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ANNALS
OF THE
RHEUMATIC DISEASES

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The Official Journal
of the
EMPIRE RHEUMATISM COUNCIL

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ANNALS

OF THE

RHEUMATIC DISEASES

THE OFFICIAL JOURNAL OF

THE EMPIRE RHEUMATISM COUNCIL

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Owing to war conditions and the need for economy in paper, two issues only of "Annals of the Rheumatic Diseases" will be published this year, instead of four; one in the Spring and one in the Autumn. Subscribers' payments will be adjusted accordingly. For the same reason, the issue of an Index to Volume One has been postponed.

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ANNALS
OF THE
RHEUMATIC DISEASES

A REVIEW OF RECENT ITALIAN WORK ON RHEUMATISM*

II.—CHRONIC RHEUMATISM

By PAOLO RAVENNA

The first Italian Institute devoted exclusively to the study of rheumatic diseases was founded in Acqui (Piedmont), a town famous for its hot springs and muds, in 1929, by the Directors of the Medical and Surgical Clinics of the University of Turin (Professors F. Micheli and M. Donati). It was enlarged and transformed into the Rheumatologic Clinic in 1932. Its clinical material includes several thousands of patients a year. Many other spas have laboratories where researches on rheumatism are carried out (Montecatini, Chianciano, Fiuggi, Abano, Salsomaggiore, etc.). Furthermore, a ward or, more frequently, an outpatient department has been devoted to rheumatic cases in the most important University Medical Clinics (Turin, Milan, etc.). There is also a vast voluntary hospital in Turin, known as the Little Home of Divine Providence, holding about ten thousand cripples, among which are numerous cases of arthritis.

Classification.—The following classification of chronic arthritis and polyarthritis was suggested by Micheli in 1929, and the most important Italian studies have been founded upon it.

1. Chronic rheumatism of known ætiology (gonococcal, syphilitic, tuberculous, pyogenic, etc.).
2. Chronic rheumatism following rheumatic fever.
3. Rheumatoid arthritis:
   - (*a*) Rheumatoid arthritis of an infective character.
   - (*b*) Still's disease.
   - (*c*) Rheumatoid arthritis with no definite infective character.
4. Osteo-arthrosis (osteo-arthritis of English authors).
5. Aseptic osteo-necrosis (Perthe's, Köhler's diseases, etc.).
6. Metabolic arthritis (gout, alcaptonuria).

* Received for publication August 2, 1939.

7. Neurogenic arthritis.
8. Traumatic arthritis.
9. Intermittent hydrarthrosis.
10. Hæmophilic arthritis.
11. Joint tumours.
12. Other, as yet unclassified, joint diseases.

This classification is, of course, only provisional. It is very similar to the one accepted by the Committee of the British Medical Association some years later (1933). It differs a great deal from the American classification, which includes only two classes of chronic rheumatic diseases: rheumatoid arthritis and osteo-arthrosis. A distinction between diseases which appear to be different in their clinical course and in their radiological and pathological pictures seems preferable because it facilitates ætiological research work, the best ground for which is a well selected and typical morbid picture. Conversely, a too-advanced unification can be dangerous both for ætiological research and for treatment.

Clinical Course.—A detailed description of the clinical course of rheumatic diseases can be found in two important publications by Ceconi,[27, 28] and in a report by Robecchi on rheumatoid arthritis.[105, 100]

Rheumatic diseases caused by a known agent may be very similar to rheumatoid arthritis, but the different ætiology is a sufficient argument to keep them separate (Micheli[82]). This group is the only one in which our knowledge is advancing on firm ground (M. Ascoli). Most frequently cases of this group are due to pyogenic streptococci. Among the rare forms may be quoted a rheumatism from malaria (Terzani and Torelli[109]).

A few words must be said on tuberculous rheumatism. Since the days of Grocco and Poncet the existence of a tuberculous rheumatism of a toxic nature, without the direct participation of Koch's bacilli, has been maintained. In more recent years these cases have been interpreted as evidence of an allergic articular reaction towards tuberculous virus or toxin (Frugoni, Ferrannini[45]). But this tendency has been steadily opposed by others, who consider such cases to be manifestations of a more or less attenuated tubercular infection of the joints. This can only be proved by finding Koch's bacilli in the affected joints and by the pathological picture which shows the common signs of any tuberculous infection (Micheli[85]). This point of view has found further support in a large number of observations by Logroscino.[65]

Syphilitic rheumatism has been studied by Casazza and Cottini,[24] G. Truffi,[111] Liuzzo,[63] Lenti.[58]

The second class of Micheli's classification considers chronic rheumatism following rheumatic fever. Chronic rheumatism due to the same causative agent as rheumatic fever is, however, according to Italian authors, an eventuality which, if at all possible, must be extremely rare (Ceconi,[28] Micheli,[82] Rensulli[96]). This class is based exclusively on the clinical evidence of cases of chronic rheumatism setting in closely after an attack, or after recurrent attacks, of rheumatic fever, in which an ætiological diagnosis is not possible. Only this could decide whether we are dealing here with the more or less casual coincidence of two diseases, rheumatic fever and rheumatoid arthritis, or whether rheumatic fever by itself can give rise to a chronic disease.

According to the above-quoted classification, there are three varieties of rheumatoid arthritis. Cases in which the disease begins with an acute episode or which in their course present acute stages, with impairment of the general condition, are included in the first group (rheumatoid arthritis of an infective character). The second group comprises cases with high fever, splenomegaly and lymph-gland enlargement of the type of Still's disease. The third group (rheumatoid arthritis of no definite infective character) includes the cases in which endogenous factors, sometimes of familial or hereditary origin, appear to be of most importance, and in which the clinical course does not show the signs of a general infectious disease. Whether these groups correspond to three ætiologically different diseases is, of course, still undecided, and is very doubtful, because their clinical courses often show variable characters according to which many cases ought to be classified first in one group, then in another. Neither radiological nor pathological findings show definite differences between them.

Spondylitis ankylopoietica is considered by Micheli and Ceconi to be a special form of rheumatoid arthritis. But its sexual incidence (more frequent in men) and its radiological signs have aroused doubts upon the correctness of this view.

Still's disease has been the object of detailed studies since the publication of a paper by Micheli and Gamna.[81] Many cases have been described: by Giordano,[52, 53, 55, 58] Gallerani,[49] Galdi, Michelazzi,[79, 80] Cassano,[25] S. Levi,[61, 62] Scardino,[107] Veritti,[115] De Filippi,[42] and others. It may be asserted that the cases

described in Italy form the most numerous group in the medical literature. It is now generally believed that Still's disease is not limited to children, as cases with the same characters have been described by the above-mentioned authors in adults. These cases presented all the features of Still's disease, with the only exception of the symptoms due to alternate growth of bone (Gralka's symptoms, etc.), which are confined to young patients.

Two cases of Felty's leucopenic splenomegaly with polyarthritis have been described by Alessandrini.[1] But most Italian authors do not recognise the autonomy of this syndrome, which has the same characteristics as Still's disease. The leucopenia, in fact, is not a deciding factor, because it is a common feature of many splenic enlargements whatever their cause. Also the cases described by Castellani[26] as febrile hepatosplenomegaly with polyarthritis have been ascribed to Still's disease (Robecchi[105]).

Spondylitis osteo-arthritica is classified as a common osteoarthrosis. All its pathological and radiological signs concurrently show a substantial identity with osteo-arthrosis of other bones.

A climacteric arthritis does not appear in Italian classifications, because an ætiological relation between arthritis and the ovaries has not yet been proved and appears to be very unlikely. Arthritis in menopause is due to climacteric changes in weight and in blood circulation, and does not directly depend on ovarian insufficiency (Pende, Micheli,[82] Ceconi,[27, 28] Robecchi,[105] Carlini[23]).

Also the clinical entity of a psoriatic arthritis has been denied, as no ætiological relationship can be established between psoriasis and arthritis (Ceconi,[29] Robecchi,[105] Micheli[82]).

Dynamic Pathology.—In Still's disease hæmatological observations have been made by Micheli and Gamna,[81] Giordano,[53] Cipriani, Robecchi and Angeleri, Pancrazio,[85, 86] De Matteis and Verdolini,[44] Mazzoni.[77] There is a frequent, but rarely very marked, leucocytosis, with absolute, and sometimes also relative, increase of neutrophils; with absolute and relative increase of lymphocytes and, at times, of monocytes. In acute stages there is a decrease or a disappearance of eosinophils. Lymphocytosis and eosinophilia are also frequent in other types of rheumatoid arthritis (Cipriani, Robecchi and Angeleri). The Arneth count is normal in latent periods; whereas it is clearly shifted to the left in active Still's disease. In osteo-

arthrosis the number of white cells is usually normal, but a relative increase of lymphocytes and eosinophils is frequent. Rieder's and Türk's cells have never been found in chronic rheumatism.

In rheumatoid arthritis the albumin-globulin ratio is close to the lowest normal figures and plasma fibrinogen is slightly increased. In uratic arthritis fibrinogen increases during attacks and is normal in latent periods. In osteo-arthrosis the ratio is normal and fibrinogen is also normal or slightly increased (Cipriani and Robecchi).

The sedimentation rate is almost constantly increased in rheumatoid arthritis. In uratic arthritis, during latent periods, its figures are generally normal even when blood uric acid is very high. The sedimentation rate increases during attacks, especially when they are accompanied by fever and marked swelling (Cipriani and Robecchi). The same authors have emphasised the importance of the sedimentation rate for the indication of stimulant physical therapy: this treatment must be delayed as long as the sedimentation rate is greatly increased.

Normal sedimentation rate has been found in 44 per cent. only of patients suffering from osteo-arthrosis. This fact is due to secondary inflammatory phenomena which very often appear when osteo-arthrosis has lasted a long time, as was the case in the patients investigated for this inquiry (Robecchi[105]).

The blood tryptophane shows the same behaviour as the sedimentation rate (Pescarmona[90]).

In some thousands of rheumatic patients the fasting blood sugar was frequently higher than normal. In sixty cases the glucose tolerance test was performed and showed delay in the rate of removal of glucose from the blood-stream. These data, which confirm those established by Pemberton, have been interpreted as being due to changes in the peripheral circulation and not to modified insular activity (Robecchi and Battistini[103]).

The increased oxalic acid level in the blood and the changes in the oxalic acid tolerance test have been considered to be consequences of the altered carbohydrate metabolism (Marcolongo and Barone,[75] Robecchi, Battistini and Quaglia,[15, 103] Di Marco[74]).

Blood calcium is not rarely increased in rheumatoid arthritis. This may depend on the rarefaction of bone, which is very pronounced in this disease. Blood calcium in osteo-arthrosis and in uratic arthritis remains within normal limits (Robecchi and Battistini[103]).

Blood phosphorus and the calcium-phosphorus ratio have normal values, according to the same authors and to Angeleri and Pescarmona.[6]

Slight changes have been noted in blood potassium, but the potassium calcium ratio is not changed (Coggi[38]).

Inquiries on sulphur metabolism have shown that the glutathione concentration in the blood is normal. The rate of oxidation of sulphur is frequently decreased, and this change is related to the gravity of the clinical condition, as it is more evident in the most advanced cases. This finding is common to rheumatoid arthritis and to osteo-arthrosis. Uratic arthritis, however, shows normal values (Battistini, Robecchi and Quaglia[11, 13, 14]).

Serum complement is frequently decreased in rheumatic fever, but it is mostly normal in rheumatoid arthritis (Robecchi, Battistini and Silvani[9, 12]).

The behaviour of the iso-agglutinating power of blood serum has been studied in various patients and in healthy individuals under different conditions (Ravenna[94]). In rheumatoid arthritis it is more or less increased, while it shows normal figures in osteo-arthrosis, uratic arthritis and fibrositis (Angeleri, Battistini and Robecchi[103]).

The functions of the superficial blood capillaries are seriously impaired in rheumatoid arthritis (Lunedei and Corradini); this fact also has been established by means of specialised techniques —*e.g.*, with the test of capillary reactions after exposure to cold— by Angeleri, Battistini and Robecchi.[5]

PATHOLOGY.—Numerous contributions to the pathology of rheumatoid arthritis have been made by Micheli and Gamna,[81] Ceconi,[28] Costa, Cassano,[25] Fieschi,[46] Galdi, Gentili,[50] Parenti,[87] Scardino,[107] Simonetti, S. Levi,[60] Tripputi, Oggioni and Toldo, Bini,[17] Magrassi.[71] Their data have been collected and completed with numerous personal observations by C. Giordano in an extensive paper published in 1937 [52] and in a very recent report.[55]

Pathological material is relatively abundant for Still's disease. But it is very scarce, especially in early stages, in the other two types of rheumatoid arthritis, on account of their very long clinical courses. Generally, lesions found at post-mortem examinations do not show the active morbid picture, but its late consequences. Pathological examination of early lesions must be confined to some tissue fragments, obtained by biopsy, or to the post-mortem examination of patients deceased from intercurrent diseases.

The descriptions of joint lesions, either in early or in late stages, are essentially the same as can be found in all modern textbooks. The fact is to be noted that the changes found in all types of rheumatoid arthritis, including Still's disease, appear to be similar and indistinguishable.

Sometimes chronic pyogenic rheumatism presents a similar pathology; but the diffuse or nodular infiltrations of synovia and periarticular tissues often contain many neutrophil leucocytes, whereas in rheumatoid arthritis the infiltration is mostly formed by lymphoid and plasmatic cells and by monocytes.

Lymph-gland lesions are very rare in rheumatoid arthritis, except in Still's disease, in which they form one of the characteristic features. Their histologic picture has been described as that of a common subacute or chronic inflammation without peculiar characters (Giordano,[53] Michelazzi,[79, 80] S. Levi[62]).

Chronic tubercular polyarthritis may show a clinical picture very similar to that of Still's disease, not only because of the aspect of the joints, but also because of the presence of a well-marked adenopathy (Giordano, Reitano). In these cases histological examination of a gland, showing the presence of typical tuberculous changes, often decides the diagnosis.

Enlarged spleen in Still's disease presents a chronic lymphatic hyperplasia, with regressive changes in the wall of the follicular vessels. When the splenic enlargement is very conspicuous there are signs of congestion and those phenomena of meso-arteritis and peri-arteritis which, according to what I maintained in a paper on the pathogenesis of congestive splenomegalies,[93] are probably the principal change responsible for all congestive splenic enlargements.

Subacutaneous nodules have the same characters in acute rheumatic fever and in chronic rheumatism. They have no diagnostic value in the differential diagnosis of these diseases, and cannot serve to ascribe both diseases to a single ætiological factor, for similar changes may be found in many specific diseases due to other causes, either infectious (frambœsia, syphilis) or not (traumatic nodules) (Ravenna,[95] Pozzo,[91] Giordano,[55] Scardino[107]).

Fibrinous or exudative pericarditis has frequently been found in Still's disease. Other cardiac changes are extremely rare.

Valvular disease, occasionally found in rheumatoid arthritis patients, can be referred to previous rheumatic fever, the clinical

course of which might have been overlooked on account of the absence of articular symptoms. Myocardial changes have rarely been found in post-mortem examinations of rheumatoid patients. Their characters differ a great deal from those of rheumatic myocarditis, because of their slight intensity and because their diffuse lymphocytic and polynuclear cell infiltrations never look like typical Aschoff's nodules (Micheli and Gamma,[81] Giordano,[52, 53, 55] Robecchi[105]).

Articular effusions show the chemical characters of exudates in rheumatoid arthritis, in osteo-arthrosis, in uratic and in traumatic arthritis. In a series of more than 1,500 arthritics, the joint effusions were shown to be frequent in Still's disease and in chronic arthritis related to trauma, while they were relatively rare in the other types of rheumatoid arthritis and in osteo-arthrosis (Cionini and Robecchi[37, 38]).

RADIOLOGY.—Lupo's important study on the radiology of chronic joint diseases, read at the 23rd Congress of the Italian Society for Hydroclimatology (Acqui—S. Remo, June 1934),[70] has been extended and published in a recent detailed article.[70a, 71] This work is worthy of note because it is based on the study of several thousands of patients (from the wards and out-patients departments of the Medical Clinic of Turin and the Rheumatologic Clinic at Acqui), as well as because of the scarcity of our knowledge on this matter.

The most important conclusions of Lupo deal with the radiologic picture of rheumatoid arthritis and its comparison with those of rheumatic fever, pyogenic rheumatism and gonococcal arthritis. According to this author the radiological changes of rheumatoid arthritis are the following:

1. Conspicuous and early increased bone transparency, which differs from disuse atrophy, because it is more homogeneous, is confined to spongy tissue and is accompanied by loss of density balance, due to a relatively increased density of the cortex (appearance " en demi-deuil " of French authors).

2. Progressive narrowing of the joint spaces, characterised by its uniform extension along the whole line of the joint.

3. Plastic, wax-like deformation of the epiphyses, caused by the shrinking of the joint capsule.

4. Lastly, destruction of the articular extremity and disappearance of the joint line and bony ankylosis.

To these changes may be added the acceleration in the ossi-

fication of carpal osseous nuclei (Gralka's symptom), which is frequently evident in infants suffering from Still's disease, but which is not characteristic of this, because it depends on the circulatory changes induced by an inflammatory process in the wrists of children.

These changes have been found in cases of rheumatoid arthritis of an infective character, of rheumatoid arthritis with no definite infective character, and of Still's disease. No differences could be found for a distinction between these diseases, except for spondylitis ankylopoietica, which is the only one that presents a different radiological picture. I have already pointed out that this is an important argument against the inclusion of spondylitis ankylopoietica in this class.

The first change to be found in spondylitis ankylopoietica is ossification in the ligaments of the vertebræ and of some large joints. This lesion precedes atrophy by a long time. Changes of true rheumatoid arthritis of the vertebræ show a quite different character—*i.e.*, marked increase of bone transparency, with accentuation of the borders of the vertebræ, which appear like reels, and lipping in their edges. This lipping may be easily distinguished from osteophytic formations.

The findings in cases of rheumatic fever are very different and, substantially, negative. The only features are: (1) Slight increase of articular spaces, probably due to effusion; (2) barely appreciable bone atrophy, which is present only in cases of very long duration and is due to inactivity; (3) inflammatory thickening in the peri-articular tissues.

Radiological changes in pyogenic rheumatism are characterised by the appearance of small, more or less circular zones of atrophy, sometimes confluent in polycyclical areas of decreased opacity. These areas are situated in an epiphysis or in the spongy bone and sometimes are surrounded by a thin halo of diminished transparency. By the confluence of the above-mentioned areas a large breakdown of bone tissue may result and then the picture becomes similar to that of other forms of chronic arthritis.

The first radiological finding in acute septic arthritis is bone destruction in the articular border, surrounded by a blended halo of demineralisation. Disuse atrophy appears secondarily.

In gonococcal arthritis Lupo has shown a characteristic change that has diagnostic value for its evidence in early stages, when the diagnosis may fluctuate between rheumatic fever and septic

arthritis. Closely beneath the thin line of increased opacity that limits the bone towards the joint cavity, a thin line of increased transparency appears; it looks as if it had been skilfully drawn. Its length is variable and sometimes it extends along the whole joint border. This peculiar aspect corresponds to the laminar sequestration which is characteristic in the pathology of gonococcal arthritis. In advanced cases this sign is less evident and the finding is similar to that of other septic arthritides.

A study of the Roentgen aspect of arthritis in undulant fever has been made by Benassi.[18]

Ætiology.—The predisposing or determining causes of rheumatoid arthritis have been sought in familial factors. Their importance is shown by the high familial incidence (about 30 per cent., Robecchi[105]). Rheumatoid arthritis has been observed in four young members of one family (two boys and two girls) by Robecchi and Pescarmona,[98] and a very rare instance of Still's disease in two brothers has been recently described by Giordano.[56]

Surroundings and occupational factors ought not to be of a marked importance in rheumatoid arthritis, because this disease is very frequent also in well-to-do patients. The often-observed rheumatism of laundry workers and rice-field labourers is due to recurrent rheumatic fever and not to rheumatoid arthritis (Robecchi[105]).

Females are more frequently affected by rheumatoid arthritis: the proportion observed by Robecchi is 35 males to 100 females.

The relationship between rheumatic fever and rheumatoid arthritis must be mentioned here, not only because of the possibility of chronic rheumatism following rheumatic fever, but also because some authors believe that true rheumatoid arthritis is always due to the same ætiological agent as rheumatic fever. This opinion has been opposed in Italy, because of the differences between the clinical pictures, the cardiac complications, the response to salicylates, the pathological pictures and numerous other reasons that have been discussed by Micheli,[82] Ceconi,[27, 28] Robecchi,[105] Andrei and Ravenna[2, 3, 95] and Giordano.[55] All these characteristics, which are not decisive when considered separately, cumulatively give very sharply defined individualities to the clinical and pathological pictures of rheumatic fever and rheumatoid arthritis. Some common histologic notes, the fibrinoid swelling and the lympho-monocytic nodules, are by no means characteristic evidence of an identical

ætiology. The importance of subcutaneous nodules has been emphasised too often (Ravenna,[95] Giordano[55]).

Endocrine glands have no direct importance in the ætiology of rheumatism (Pende, Ceconi,[28] Micheli[82]). The pathology of the parathyroid glands and the results of their removal or of more or less superficial operations in the neck has been frequently studied (Francaviglia, Bendandi,[19] Conti,[39] etc.); they have been inconsistent, and the prevalent opinion is that the clue to the right understanding of chronic rheumatism is not to be found there (Micheli,[82] Robecchi,[105] Usseglio[114]).

Excluding some well-known metabolic forms of arthritis (gout, alcaptonuria), no definite importance has been given to abnormalities of nutrition. The importance of malnutrition in the pathogenesis of osteo-arthrosis has decreased, while the value of hereditary, traumatic and local circulatory factors has increased (Robecchi[105]).

Nervous factors undoubtedly have a determining importance in some arthritides. These are considered in a special class, which includes tabetic arthritis and other joint deformations accompanying nervous diseases. Among these are the joint changes of encephalitic parkinsonism, which have been studied by Pennacchietti.[89] But the coincidence of nervous changes with rheumatoid arthritis is too rare for the admission of any relationship between these diseases (Robecchi[105]). Neither can osteo-arthropathia micro-atrophicans (Blum) be referred to nervous changes (Usseglio and Ceresa,[113] Ceconi [27, 28]).

Bacteriology has decided the ætiology of all the rheumatic diseases which are included in the class of rheumatism due to a known ætiological agent. The causative agents (streptococci, staphylococci, gonococci, Koch's bacillus) have been found in affected joints. This fact not only explains the ætiology, but also shows the inconsistency of any theory that tries to explain these joint lesions as a toxic or allergic mechanism.

In rheumatoid arthritis, including Still's disease, bacteriological examinations have been very numerous; but results have been negative, with few exceptions (Gallerani,[49] Corelli[40, 41]). These researches have been carried out on joint fluid, or synovial and peri-articular tissues, surgically removed during acute phases, and on regional glands and subcutaneous nodules (Giordano[51, 52, 54]). The prevalent opinion is that rheumatoid arthritis is a true infectious disease: the fact that the causative agent has not yet been found does not mean that it does not exist, but that

it is still undiscovered (Micheli[82]). The negative bacteriological findings in Still's disease are one of the strongest arguments against the acceptance of a causative agent common to this disease and sepsis lenta such as the *Streptococcus viridans*. A marked difference between these diseases has been established also from the clinical view-point (Micheli[81, 82]).

Numerous investigations have been made to explain the constant failure to discover germs in joints affected by rheumatoid arthritis, while refusing to deny an ætiology by known bacteria. Many experiments are related to the so-called allergic-focal infection. According to this theory a focus of localised infection might induce a bacterial hypersensitivity in the organism and entry into the circulation of bacterial toxins might provoke the morbid picture of rheumatoid arthritis as the result of a general anaphylactic reaction. I have already summarised the results of these experiments, which are in part related to the ætiopathogenesis of rheumatic fever. They have yielded no proof to support the role of allergy, because the experimental lesions have always been found in tissues where the presence of germs could be demonstrated or might have been demonstrated (Andrei and Ravenna,[2, 3] Magrassi). The pathological comparison between experimentally induced changes and the lesions of human rheumatic fever has made it possible to exclude an identity or even a close similarity. In rheumatic fever this comparison is relatively easy on account of its typical pathology (Ravenna[95]). The pathology of chronic rheumatism is not so sharply defined or so characteristic, and every morphological comparison is, therefore, difficult and undecisive. The question of an eventual allergic origin must be resolved on other bases. Neither have instances of experimental arthritis induced by injection of foreign protein yielded results applicable to the pathogenesis of rheumatoid arthritis (Locatelli, Barbiroli[7]).

Interesting advances have been made in the ætiopathogenesis of gout. The investigations can be divided into two groups; the first deals with the general pathogenesis of gout and the second with the pathogenesis of the arthritic attack. The summary of the work done in the first group would be too lengthy; these researches deal with the renal insufficiency, the hypertension and the gastric anacidity of gouty patients (Battistini, Robecchi, Quaglia and Pescarmona[10, 16, 101, 105]). The second group has shown suggestive results on joint pathology. Uric acid has a peculiar tropism for joints; it is a very modest phlogogenous

agent, but it can strengthen the inflammatory potency of other substances. Allergic phlogosis is greatly reinforced by uric acid (Rondoni). This fact is probably a consequence of its power to increase the permeability of membranes (Chini). In experimental animals an allergic phlogosis due to intravenous injection of foreign protein in a previously sensitised animal can be localised in a joint by means of a preparatory introduction of uric acid (Chini). Various papers by Chini[31] and an interesting review by Robecchi[102] deal with the practical value of these findings, which go to show that the attack of gout is due to an allergic reaction towards different allergens, probably of alimentary origin, and that this reaction is localised in joints by the uric acid.

TREATMENT.—The therapy of chronic rheumatism is based upon hygienic treatment and sometimes on diet (Pisani[90] got satisfactory results with Pewsner's desensitising diet); upon anti-infective agents (general stimuli—proteinotherapy and chemotherapy, and local stimuli—histamin and similar poisons, and also the Chinese acupuncture which has recently been tried by Vinai[116]); upon topical drugs, physical treatment and orthopædic procedures. A recent review on the therapy of rheumatism has been published in the *Gazzetta Medica Italiana*, 1938, vol. 97, no. 12 (December).

Surgical removal of foci of chronic infection (teeth, tonsils, appendix, gall-bladder, prostate, etc.) has not aroused the same enthusiasm in Italy as in other countries. This matter, however, has been the object of extensive observations by the Schools of Professors Frugoni (Rome), Micheli (Turin) and Azzi (Turin). Their principal results have been collected in a Report on Focal Infections, read by Lusena and Chini at the 39th Congress of the Italian Society for Internal Medicine, Pavia, October, 1933; in a synthetic report by Frugoni;[48] in many experimental studies by Andrei and myself,[2, 3] Mela,[78] Lucca,[67] Spina[108] and Chini;[32, 33, 34, 35, 36] and in a recent detailed review on connections between tonsils and internal diseases by Chini.[30] From the therapeutic view-point the prevalent practice is to remove chronically inflamed organs only when they are, by themselves, a direct cause of disease (Micheli,[82] Ceconi,[28] Malan).

This does not exclude the possibility of cases of pyogenic rheumatism caused by germs entering the blood-stream from a chronic infective focus. But the spread of germs from an acute inflammatory process, where the focus has not yet become circumscribed, is likely to be a more frequent eventuality. Whether

the removal of the primitive focus of infection can cure the rheumatism is an unresolved question; but it is difficult to understand why germs living in joints or in peri-articular tissues should not be able to grow and to multiply after the removal of the so-called foci, and why the joint disease should need a continuous supply of germs from the primitive focus.

Inflammation of the tonsils or of another organ can be followed by a recurrent attack of a latent or healed rheumatism. But this does not imply a common ætiological agent. The massage of inflamed tonsils can induce a new acute articular attack; the same results can, however, be obtained in the same patients with any protein shock, with a milk injection for instance, where all infective mechanisms can be excluded. The positive result of the tonsillar massage (the so-called tonsillar-test) demonstrates no more than the existence of foreign protein in the tonsillar tissue (Robecchi, Olivetti and Malan[84]).

Also the successes that sometimes have been obtained with vaccine therapy are probably due to non-specific stimulotherapy and do not prove an ætiological connection between the injected germs and the rheumatism (Corelli,[40, 41] Fieschi,[46] Usseglio,[114] Andrei and Ravenna[3]).

The same conclusion has been drawn from the clinical observation on many patients who have already been deprived of all possible foci of chronic infection and yet do not show a more favourable clinical course than others (Micheli[82]).

Oily suspensions of gold salts give very good results which it is impossible to obtain with other methods in the treatment of rheumatoid arthritis. The action of gold salts is not strictly bound to the dose and should not be confined to a shock therapy. Notwithstanding its well-known dangers, such a therapy forms the best means at our disposal for the treatment of chronic rheumatism (Angeleri, Battistini, Robecchi,[4] Usseglio,[114] Finazzi,[47] Galdi).

A new method in the treatment of arthritis was employed by Rinaldi, a physician in a small village near Siena (Tuscany). His method was kept a secret, but was published after his death, following an inquiry by the Department of Health of the Italian Home Office (Marotta, Lazzarini and Calò[76]). Rinaldi's method consisted essentially in injections of strong doses of sodium glycerophosphate, together with small doses of sodium cacodylate and strychnine. It has been tried by Lucherini,[68, 69] Usseglio,[114] Caccuri,[22] Del Prete,[43] M. Levi,[60] Sartori[106] and others, who gave intravenous injections of 10 c.c. of a solution containing

2·5 grammes of glycerophosphate in distilled water. This method has been employed in all chronic rheumatic diseases. Daily injections must be given for 20 days. This treatment has an evident and rapid action on pain and swelling; the patients also feel better and their appetites increase manifestly; they become euphoric, feed more abundantly and the movements of affected joints improve. These results can be obtained in a few days, but they are only temporary. Since this treatment appears to be harmless, it can be employed in everyday practice even though it does not produce the miraculous effects that had been claimed. After all, we do not yet know of any other miraculous treatment of arthritis.

Studies on mud-therapy have been made by Peserico and Pisani. A recent review of its results, stating indications and contra-indications in rheumatic patients, has been published by Quaglia.[92] As mud-therapy acts as a lively stimulus, its use must be carefully delayed during acute periods, both in rheumatism and in gout. The sedimentation rate may be very helpful in indicating the right time for beginning the treatment. The effect of this therapy on uric acid metabolism has been studied by Comel, Barengo[8] and Jandolo.[57] The variations of complement in the blood during mud-therapy have been studied by Robecchi, Battistini and Silvani.[12]

Among other therapeutic attempts that have had a limited or unconfirmed success I would mention the injection of cerebrospinal fluid in chronic arthritic patients (Negro) and the intraspinal injection of phenolsulphonaphthalein (Boschi[21]).

In the local treatment of arthritis, histamin has been used with success (Negri,[83] Jacchia) and good results have been claimed with intra-arterial injection of gentian violet (Lucarelli[66]) and with novocain infiltration of the peri-articular tissues (Tripodi,[110] Mansione and Bugliari[73]) in mono-articular arthritides.

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RECENT INVESTIGATIONS ON RHEUMATISM AND ARTHRITIS IN THE UNITED STATES*

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The incidence of "rheumatism and allied diseases" on a given day in the United States has been estimated[114] to be about one case (0·099 per cent.) per 1,000 persons. The incidence according to age and sex per 1,000 persons was as follows: less than ·05 case among persons less than fifteen years of age; 0·9 among those aged fifteen to sixty-four years, and 5·4 for those aged sixty-five years or more. The incidence for females was twice that for males. In the arthritis clinic of the Presbyterian Hospital, New York, the percentage incidence of the commoner forms was about as follows: osteo-arthritis 30, rheumatoid arthritis 25, non-articular rheumatism 20, traumatic and postural arthritis 10, rheumatic fever 5, gonorrhœal arthritis 3, gout 1, miscellaneous 6.[45]

Gonorrhœal Arthritis

Despite efforts of national and civic bodies there is as yet no significant reduction in the incidence of gonorrhœa in the United States. According to a recent survey [115] the incidence per 1,000 population varied from a maximum of 46·6 white males, 69·9 negro males, 15·1 white females and 46·5 negro females to a minimum of 2·3 white males, 6·6 negro males, 0·2 white females and 2·2 negro females in various American localities. The incidence of gonorrhœal arthritis among cases of gonorrhœa is generally considered to be about 2 or 3 per cent.

Diagnosis.—The frequency and diagnostic significance of certain lesions of the skin which may accompany gonorrhœa and gonorrhœal arthritis have been emphasised again.[54, 61] The lesions include petechiæ and small red sore spots sometimes with a central white necrotic region. "The clinical lesion in full development is a hæmorrhagic, purulent vesicle or bulla, surrounded by a more or less broad erythematous areola." The hemorrhagic feature may be absent. Those concerned with

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diseases of joints should familiarise themselves with this lesion because it has been noted in cases of gonococcæmia and gonococcal arthritis, in which careful search revealed no culturally positive genital focus although gonococci were present in joints and in some of the cutaneous lesions.

In cases of chronic gonorrhœa cultures for gonococci are notably superior to direct smears, according to many investigators. But in 8 per cent. of one series of cases[18] cultures were negative and smears were positive; hence both tests should be used when possible. Some physicians[48] consider complement fixation tests superior to cultures or smears, but others[50] have concluded that the fixation test as generally performed is of limited usefulness and needs further refinement and standardisation.

Treatment.—The two most effective remedies continue to be fever therapy and sulfanilamide or allied compounds used alone or together. Results of fever therapy in about 560 cases of gonorrhœal arthritis were reported.[45] Complete cures were obtained in 70 to 90 per cent. of acute cases and in about 60 to 80 per cent. of chronic cases. From two to four, sometimes six to eight, sessions of fever were given, most of them consisting of five or six, occasionally seven, hours at 106 to 107° F. (rectal) given every two to four days. With fever therapy, cures were obtained eleven times as often as with older methods (local chemotherapy, physical therapy) in cases of acute gonorrhœal arthritis, and six times as often in chronic cases.[92] Fever therapy generally controlled both the articular and genital infections; but sometimes the latter were resistant; hence several physicians[9, 59, 82] favoured the use of fever combined with pelvic diathermy and reported prompt clinical and bacteriologic cures often after the use of only one ten-hour session.

Fever therapy, given in a hospital by a trained staff, is essentially safe. During the administration of about 5,700 sessions of fever therapy to more than 1,200 patients, only two deaths occurred.[57, 59, 112] A few other untoward reactions were noted: minor burns, abdominal pains, cardiovascular collapse and two additional deaths, one of which was the first reported among children.[34] Despite its effectiveness fever therapy is admittedly a time-consuming, uncomfortable and strenuous ordeal, a procedure available to only a small percentage of gonorrhœal patients. Hence it should be reserved for those whose disease is not amenable to the newer chemotherapeutic agents.

Among the scores of papers[45] on the effect of sulfanilamide on gonorrhœa which were reviewed for this synopsis were data on only fifty-four cases of gonorrhœal arthritis: in thirty-eight (70 per cent.) of these fifty-four cases the arthritis was rather promptly cured; in sixteen cases (about 30 per cent.) it was unimproved, or improved but not completely cured by the drug. One report[7] was concerned with the treatment of fourteen patients with proved, and four with " probable," gonorrhœal arthritis with " large doses " of the drug (daily dose, $\frac{3}{4}$ grain or 0·05 gm. per pound of body weight, but not more than 120 grains or 8 gm. in one day). Nine (64 per cent.) of the former and two (50 per cent.) of the latter patients, that is, 61 per cent. of the total, were " strikingly improved " forty-eight to seventy-two hours after treatment was begun. Infected synovial fluids became sterile promptly, and no gonococci were present in genital foci after three days of medication. No relapses occurred. The effective dose varied greatly: some cures were effected with 5 mg. per cent. of free sulfanilamide in blood; in other cases 10 mg. per cent. or more was required. If definite clinical improvement was not noted seventy-two hours after starting " large doses," the doses were increased. To maintain a constant level of free sulfanilamide in blood, one-sixth of the total daily dose was given every four hours, day and night, and the fluid intake was kept constant.

Doses of sulfanilamide used by others in the treatment of gonorrhœal arthritis were: in one clinic,[95] daily, 80 grains (5·2 gm.) for two days, 60 grains (4 gm.) for two days, and 40 grains (2·6 gm.) for seven days; in another clinic,[25] daily, 75 grains (5 gm.) for two to three days, 60 grains (4 gm.) for two to three days, then 40 grains (2·6 gm.) for the remainder of a fourteen-day course. Although the full doses originally recommended by Long (1937) and by Colston, Dees and Harrill (1937) were used occasionally, in most cases gonorrhœa and gonorrhœal arthritis were treated by smaller doses. The true value of sulfanilamide in the control of gonorrhœal arthritis can be determined only by treating with full doses many more patients who are known to have gonococci intra-articularly.

A statistical summary of forty-six recent reports on the use of sulfanilamide for urogenital gonorrhœa was made.[45] Of 2,293 cases of gonorrhœa noted therein, cure was presumably effected in 67 per cent. (1,540 cases). Many of the patients were

ambulatory and were not subject to as close supervision, nor as tolerant of full doses of the drug, as hospitalised patients. Among the reasons for failure to obtain cures in some cases were the inability of about 10 to 20 per cent. of patients to take adequate amounts of the drug, use of insufficient doses for those who could take full doses, premature cessation of treatment, stopping of medication when symptomatic cure resulted but before bacteriologic cure was obtained, and the resistance of certain patients, or their strains of gonococci, to sulfanilamide. In general, however, dramatic results and very prompt and satisfactory cures were noted. Therefore it seems probable that regardless of whether the incidence of genital gonorrhœa is notably reduced or not, the incidence of gonorrhœal arthritis will be markedly lowered as more and more patients are given sulfanilamide or allied compounds early. In a series of papers which concerned about 2,247 cases of gonorrhœa treated with sulfanilamide, mention was made of only thirty-one cases of gonorrhœal arthritis: the expected incidence of gonorrhœal arthritis among that number of cases of gonorrhœa (at a rate of three per 100 cases) should have been sixty-seven instead of thirty-one cases. This observation suggests that already the incidence of gonorrhœal arthritis has been notably reduced, and is the basis for the, perhaps unduly optimistic, prediction of some physicians that gonorrhœal arthritis may practically disappear.

This type of treatment has many advantages: the drug is cheap, easy to use and essentially non-toxic, and it promptly cures about 70 per cent. of patients with gonorrhœal arthritis, even though it must often be given to ambulatory patients for whom the dosage cannot be controlled satisfactorily. Its disadvantages, however, are becoming more obvious. It provokes annoying reactions commonly, and serious, even fatal, reactions occasionally.[45] Effective doses cannot be taken by 10 to 20 per cent. of patients, and it has failed to cure in about 30 per cent. of cases of gonorrhœal arthritis. Therefore several physicians[45] have combined the use of sulfanilamide with older forms of local chemotherapy or with fever therapy. In a number of cases, gonorrhœal arthritis, which had proved resistant either to fever therapy or to sulfanilamide when used alone, was cured promptly by the combined form of treatment.[29, 88, 95] Some physicians[20] prescribed 80 grains (5·2 gm.) of the drug daily for two days prior to fever therapy (generally one ten-hour session at 106° F.).

Others[95] gave 40 grains (2·6 gm.) of the drug daily for three days, then ten hours of fever at 106° F. or 60 grains (4 gm.) the day before a fever session of seven hours at 104 to 105° F.[5] It was recommended[25] that patients who are not relieved of gonorrheal arthritis by three to six days of treatment with sulfanilamide should be promptly subjected to fever therapy.

Tuberculous Spondylitis

Do fusion operations shorten the course of tuberculous spondylitis and prevent deformity? After making a careful, "unprejudiced" ten-year study, a group of physicians[33] answered this question in the negative. One group of twenty-six patients was treated by fusion operations, generally of the Albee type. Another group of seventeen patients, closely parallel as to age and the duration, severity and situation of their disease, received conservative measures: rest on frames, good food, sunlight, fresh air, and so forth. The surgical group required 40 per cent. *more* time (average, 1,215 days) for cure than the non-surgical group (average, 876 days). The operation seemed to prolong, rather than shorten, the course of the disease. Despite firm fusion the disease in the vertebræ seemed uninfluenced: in each group about the same number of abscesses, paraplegias, recurrences and spinal deformities developed.

Pneumococcal Arthritis

Pneumococcal arthritis, a rare disease, will probably become rarer as a result of the use of the newer sulfonamide compounds. No instance of pneumococcal arthritis was noted among the numerous cases of pneumococcal infections so treated and reviewed for this report.[45]

Syphilis of Joints

"Arthralgia" develops in about 5 to 10 per cent. of cases of early syphilis; syphilitic synovitis or arthritis in about 1 per cent. The commonest form is "Clutton's joint," bilateral synovitis with hydrops of knees among congenital syphilitics.[68] Syphilitic synovitis occurs more often in late cases of acquired syphilis. For it synovectomy was considered useful. Gummatous arthritis occurs only in tertiary syphilis; according to some[96] it may closely resemble rheumatoid arthritis, an idea not concurred in by others.[68] In about 4 per cent. of cases of

tabes Charcot joints develop; new cases were described.[45] An improved technic for arthrodesis of Charcot joints was described:[98] multiple bone drillings of involved articular bones to improve vascularity and osteogenesis; immobilisation for four to six weeks by a posterior plaster splint; then standard arthrodesis.

Brucellosis: Undulant (Malta) Fever

Symptoms Referable to Muscles and Joints.—It is agreed that "joint pains," "pains in limbs," "rheumatic pains in back and joints" and "pains in muscles of arms and legs" are common features of brucellosis, but there is no agreement as to the incidence of true acute or chronic arthritis from brucellosis. Brucellosis is particularly common in the south-western part of the United States, and certain physicians[35, 69, 85] there have reported that the disease commonly masquerades as rheumatoid arthritis. Physicians elsewhere are inclined to believe that most of these cases probably represent ordinary rheumatoid arthritis coincidentally present in cases of latent, sometimes of active, brucellosis.

Diagnosis.—Opinions still differ as to which of the various laboratory tests is most helpful in diagnosis; in general the agglutination test was favoured.[45] A negative result, however, does not prove the absence of the disease; in almost half of one series of chronic cases negative reactions were obtained. Certain experiments[117] indicated that sulfanilamide markedly increases opsonocytophagic activity for Brucella organisms, and in some cases of brucellosis agglutination tests gave negative results before administration of sulfanilamide and positive results afterward.

Treatment.—Results of the use of serums, typhoid vaccine and certain "specific vaccines" seemed satisfactory to some physicians, unimpressive to others.[45] In 81 per cent. of twenty-one cases of brucellosis in which treatment consisted of artificial fever (five to twenty-two hours) cure occurred,[81] but sulfanilamide appears to be the most promising remedy. Striking recoveries followed its initial use by eight patients treated in Europe, some of whom may have been entering a period of remission or recovery when treatment was begun. The further experience of American clinicians confirms that of English workers and seems to indicate that the drug is truly effective. Twenty recent reports[45] gave results from the use of the drug in sixty cases of acute and chronic brucellosis: 87 per cent. of the patients were "cured"

generally within four to seven days. Usually the drug was given orally in doses ranging from 60 to 75 grains (4 to 5 gm.) daily for about nine days, to 35 grains (2·3 gm.) daily for about ten days.[45, 111, 117] Because relapses occurred occasionally, some physicians advised the routine use of one to three follow-up courses, each a week long, within two or three months of " a cure."

Meningococcic Arthritis

The incidence of articular lesions in meningococcic infections has varied from 4·8 to 20 per cent. in different epidemics; it was recently 7·7 per cent. at Bellevue Hospital, New York. Details of twenty-three new cases were reported.[90] Articular lesions were classified thus: (1) An early, often pre-meningitic, polyarthritic or arthralgic form attributable to peri-articular and intra-articular petechial hæmorrhages in which the general prognosis is poor and that of joints is good; (2) the usual post-meningitic form, which generally appears after the fifth day of the general infection, is purulent and may produce irreparable articular damage; (3) a serous type resembling serum sickness; and (4) occasional post-meningitic spondylitis which may represent a true meningococcal entity, or in some cases may result from damage to discs from repeated spinal puncture.

Articular lesions were treated by aspiration, splinting and occasionally by traction. The general infection was treated by serum and Hoyne's antitoxic-antiserum, or by sulfanilamide. The latter seemed to be as effective as, in some cases more effective than, serum. Among 205 patients with meningococcic meningitis (none with arthritis) recently treated by sulfanilamide alone or in combination with serum there were only seventeen deaths.[45]

Articular Disease caused by Hæmolytic Streptococci

Formerly a fairly large proportion of cases of septic arthritis was due to hæmolytic streptococci, but since the advent of sulfanilamide this type of septic arthritis already seems to be disappearing. Only one instance of this complication was noted among many recent reports of conditions attributable to these bacteria: perfect function was obtained in a septic knee after use of sulfanilamide and aspiration.[17] This illustrates the supreme importance of making bacteriologic diagnosis as often and as early as possible in all cases of acute (septic) arthritis.

Arthritis of Scarlet Fever: Post-scarlatinal Rheumatism

Opinions vary as to the value of sulfanilamide in scarlet fever; some say that it has no effect on fever, toxæmia or incidence of complications, but others[89] noted a reduction in the incidence of arthritis in patients given the drug.

Rheumatic Fever

Clinical Data.—Noted in one group of rheumatic patients was a familial tendency manifest for at least three generations which strongly suggested constitutional susceptibility to the disease.[84] Rheumatic symptoms affected four times as many siblings, four times as many parents, twice as many uncles and aunts, and eight times as many grandparents of thirty-three rheumatic children as they did those of thirty-three non-rheumatic children. Within two weeks each of identical twins came down with rheumatic fever and mitral endocarditis.[73] Rheumatic fever frequently may attack children earlier than has been suspected: in the fatal case of an infant thirty-two months old, the disease apparently began at the age of eighteen to twenty-four months.[28]

Clinical data on new series of cases were reported.[4, 63] Polyarthritis and carditis respectively affected 135 and 122 of one group of 150 patients whose average age was eighteen years.[4] An unusual complication in one fatal case was rectal temperature of 109° F.[12] In Philadelphia in 1936 the mortality rate for rheumatic carditis was 17·6 per 100,000 population when " probable cases " were excluded and about 25 to 30 per 100,000 population when they were included. The mean age at death was 36·5 years.[40] The incidence of rheumatic carditis among 104,163 students at eighty-six American colleges and universities was 11·6 per 1,000 (9·5 per 1,000 men, 14·9 per 1,000 women).[39] Calcareous aortic stenosis occurs much more frequently than has been supposed, and is unquestionably a rheumatic lesion.[22, 119] The argument on the specificity of subcutaneous rheumatic nodules has continued. One investigator,[67] using supravital stains, regarded the nodules as very similar to, if not identical with, nodules from patients with rheumatoid arthritis, but another physician[55] noted enough differences for him to differentiate them. Physicians agree on the type of pathologic reactions

found in lungs, but disagree as to whether or not they are specific for rheumatic fever: one writer[70] considered the pulmonary reaction not of the simple inflammatory type (bacteria and necrosis are absent) but a hyperergic one; another writer regarded "rheumatic pneumonia" as possibly an important factor in subsequent failure of the right ventricle.[36] A thorough review of rheumatic erythema appeared.[55] Contrary to older opinions, erythema annulare rheumaticum may occur as an initial symptom of rapidly fatal rheumatic fever.[3] Recent literature has included descriptions of a variety of so-called rheumatic abdominal symptoms.[27] Their significance will be uncertain until a pathologic explanation for them is forthcoming. New statistical studies were made on the course of rheumatic fever and on the manner of death therefrom; unfortunately they afforded no grounds for lessening one's pessimistic attitude toward this disease.[11, 13, 51]

Laboratory Data.—It was noted that hypocholesterolæmia accompanies acute rheumatic fever and rheumatic carditis frequently, but not always.[75, 78]

Ætiology.—Further data have been suggestive of, but have not proved, a relationship between rheumatic fever and nasopharyngeal infections caused by hæmolytic streptococci.[45] The hypothesis of bacterial allergy as the cause of the disease is accepted by some, severely criticised by others. Further evidence was reported[53, 87, 94] indicating that patients with active or quiescent rheumatic fever have subnormal amounts of vitamin C in their serum, but it is difficult to interpret these data: it is possible that most rheumatic patients are simply on a deficient diet, or that the disease depletes their blood of the vitamin, and the deficiency, therefore, is the result, not the cause, of the disease;[94] or that the deficiency represents an inherent or acquired metabolic fault which may be an integral factor in the causation of the disease.[87]

Treatment.—There have been no outstanding new developments in treatment. Despite the supposed relationship between rheumatic fever and hæmolytic streptococci, sulfanilamide seems to have no beneficial effect on the course of any features of the disease. Two groups of eight and fifty-eight patients in all stages of the disease were treated.[66, 102] No benefits were noted; indeed, symptoms were often intensified and marked toxæmia was noted. Sulfanilamide may prove more useful in the pre-

vention of rheumatic exacerbations due to acute hæmolytic streptococcal pharyngitis than in the treatment of the disease. Following the use of neoprontosil, throat cultures of carriers of hæmolytic streptococci frequently became negative.[46] Of special interest are two reports[23, 107] concerning 110 rheumatic patients who received from 15 to 30 grains (1 to 2 gm.) of sulfanilamide daily from November to June: hæmolytic streptococcal infection and significant rheumatic exacerbation developed in only one case; controls were more frequently affected. No notable reaction to the drug occurred.

Tonsillectomy and the use of vaccines and serums continue to yield equivocal results.[45] Use of vitamin C does not prevent or cure the disease,[53] but the increased need of rheumatic patients for this vitamin should be recognised and supplied. Fever therapy seemed to reduce symptoms and shorten the attacks in a few cases.[95] It did not harm the heart; indeed, cardiac improvement seemed to occur in some cases,[76] but the patients have not been observed long enough to note whether the course of the carditis was really affected.

Sydenham's Chorea

For a century a close relationship generally has been thought to exist between chorea and rheumatic fever, but just what the relationship is has been solved by neither bacteriologic nor pathologic researches. According to some, no structures resembling rheumatic nodules have been found at necropsy in cases of pure chorea; but one physician recently noted perivascular nodules resembling Aschoff bodies in the brains of patients dead of chorea.[93] Because of the frequency with which pain of muscles and joints, frank rheumatic attacks and carditis developed among 467 patients with chorea, other physicians[100] regarded chorea not only as a manifestation, but a major manifestation of rheumatic infection.

Further reports[31, 76, 91, 100] attested to the superior value of fever therapy for this disease. One group of ninety-nine choreic children, given fever therapy, thereafter had polyarthritis much less frequently, carditis and recurrent chorea somewhat less frequently than did a group of sixty-six choreic children treated otherwise.[100] Sulfanilamide was valueless in the treatment of seven cases.[66]

Rheumatoid (Atrophic) Arthritis

Clinical Data.—Details concerning three new series of cases were reported.[15, 60, 110] Among 1,765 patients with rheumatoid arthritis shoulders were affected in only 9 per cent.[60] Symptoms referable to the shoulders were out of proportion to roentgenographic changes, which were rarely marked. Rheumatoid arthritis of shoulders tends to be bilateral; it usually progresses slowly, generally without the exacerbations which affect weight-bearing joints, and often almost painlessly, to a stage of marked limitation unless early vigorous treatment is instituted.

Attention is being paid to two special clinical features, the effect of jaundice[41, 108] and of pregnancy[42, 45] on rheumatoid arthritis. Coincident with the development of intra-hepatic or obstructive jaundice, remissions in articular symptoms occurred in nineteen cases and lasted from five to eighty-two weeks. (Remissions lasting from four to 104 weeks occurred in nine cases of primary fibrositis and jaundice.) Relief of pain was complete in 63 per cent. of the arthritics, in all of the fibrositic cases; relief was notable but incomplete in 37 per cent. of the arthritic cases. Active articular swelling, muscular stiffness, soreness and fatigue also were reduced markedly or had disappeared, but residual articular thickening and stiffness from deformity were of course unaffected. As one person said, " When the jaundice came in the front door, the rheumatism went out the back door." The duration and completeness of remissions bore a general, but not a specific, relation to the intensity and duration of jaundice. Mild jaundice was ineffective. The phenomenon was evoked in rheumatoid arthritis by several types of jaundice, but it was not evoked when jaundice affected patients with certain other painful types of articular and neuritic diseases. Apparently in rheumatoid arthritis the phenomenon usually does not, but occasionally may, accompany jaundice from chrysotherapy.[45]

Pregnancy has long been considered dangerous for arthritic women because disease of the joints is likely to flare up after parturition. Physicians[42, 45] recently have concluded that, regardless of the aftermath, pregnancy, like jaundice, initiates a physiologic state decidedly beneficial, at least temporarily, to patients with certain articular diseases, notably rheumatoid arthritis. The effects of thirty-seven pregnancies on twenty-two

patients (sixteen with rheumatoid arthritis, two with psoriatic arthritis, two with peri-articular fibrositis, one with intermittent hydrarthrosis and one with localised lumbar arthritis, presumably infectious) were studied. Twenty of the twenty-two patients obtained marked, generally complete, relief of articular symptoms during pregnancy and for variable periods thereafter. These twenty patients had thirty-four pregnancies, in thirty-three of which the phenomenon of relief appeared; it did not appear in a case of early tubal pregnancy, nor did three pregnancies favourably affect the arthritis of two additional women. With variations, the remissions generally began about the fourth week of pregnancy and lasted about four to six or more weeks after parturition. Several patients noted relief on repeated pregnancies, in one case during each of nine pregnancies.[45] It seemed reasonable to suppose that the agents responsible for both of these phenomena (relief from pregnancy and from jaundice) are closely related, perhaps identical. "If the potent common denominator of these two phenomena can be discovered, progress in treatment may be expected." Meanwhile it becomes obvious that rheumatoid arthritis (and fibrositis) can no longer be regarded as necessarily relentless, uncontrollable diseases for which no rapid method of control should ever be expected. The pathologic physiology of these diseases is apparently rapidly reversible. It behoves physicians to learn how to stimulate in a practical way the beneficial mechanism so effectively stimulated temporarily by jaundice or pregnancy.

Instances of three features rarely associated with rheumatoid arthritis were reported:[45] "opera glass hand" (*la main en lorgnette* of Marie and Leri), scleromalacia perforans and diabetes with resistance to insulin.

Pathology.—The focal collections of round cells commonly seen in synovial membranes in rheumatoid arthritis are considered by some to be specific for this disease, by others to be non-specific. Recent writers[47,52] favoured the latter view.

Laboratory Data.—Arguments for and against the infectious theory were summarised.[44] The rôle of infected foci has not been clarified. A former strong advocate of focal removal reported[20] his discouragement at the results thereof: of his 200 consecutive patients with rheumatoid arthritis, 70 per cent. had no demonstrable foci, 10 per cent. had doubtful foci, only 20 per cent. had definite foci, and only a few patients were improved

by removal of the definite foci. "As far as typical rheumatoid arthritis is concerned, it would appear that chronic focal infection plays a comparatively unimportant rôle." Others took a less positive stand.[45] Still others[77] repeated their view that many of the symptoms of this disease arise from disturbances of peripheral circulation and can be alleviated by correction of the latter. Some physicians[86, 94] continue to regard a deficiency of vitamin C as an important ætiologic factor, but have adduced no conclusive evidence thereof.

Treatment.—The conservative removal of obviously infected foci was generally recommended, not as a cure, but to improve the patient's general health. Vaccine therapy seems to be finding fewer champions; good results were noted by some physicians, but the majority considered vaccines of very limited value. Injections of chaulmoogra oil found little favour.[45, 97] Bee venom therapy received only faint praise,[58] and results from actual bee stings were "discouraging."[74] "Encouraging," but not striking, were the results from the intravenous and oral administration of ascorbic acid.[86] Massive doses (80,000 to 160,000 U.S.P. units) of vitamin D were given daily to two groups totalling forty-seven patients; the majority were not improved; a few noted transient subjective improvement.[2, 99]

Chrysotherapy is being investigated in several research clinics, but reports of results are not yet generally available. In one series of cases[110] preliminary results were "disappointing," but no details were given. Others[56] considered chrysotherapy of distinct value. Sulfanilamide has proved to be valueless.[7, 95]

Various attempts have been made to reproduce the analgesic effect of spontaneous jaundice by using bile and related substances. No significant results were noted by one physician[41, 43] from the use of natural or synthetic bile salts, human bile, ordinary liver extracts, transfusions of jaundiced blood and experimental jaundice induced by toluylenediamine. Other physicians[108, 109] observed no beneficial effect from the intravenous use of either bile salts (decholin) alone or bilirubin alone, but they reported that injections of the two together in fairly large doses daily for seven to twelve days produced an ameliorating effect. Of sixteen patients so treated fourteen experienced variable amounts of relief lasting from only a few days to several months. Elsewhere,[43] however, the work could not be satisfactorily corroborated. Twelve patients received from twelve to thirty daily intravenous

injections of bilirubin and decholin. Despite the production of a notable pigmenting hyperbilirubinæmia, little or no relief was noted in five cases, short incomplete remissions resulted for a few days only in six cases; one patient had a rather complete remission of symptoms lasting only three weeks. The procedure is still experimental, but the fact that the disease could be modified at all by such a novel method seems significant. The matter deserves further consideration.

Still's Disease

Clinical and pathological features were reviewed.[45, 80, 105] In only about twenty cases have data obtained at necropsy been reported; such data concerning several new cases were noted.

Primary Osteo-arthritis

" Osteo-arthritis of the same type seen by every radiologist today " affected the bones of a mastodon of the Post-Pleistocene Age recently found in North Carolina.[21]

Ætiology.—Recent discussions on ætiology were mostly restatements of the usual ideas, and no striking new evidence for any one theory was presented. Metabolic rates are generally normal;[83] concentrations of vitamin C in blood are not deficient.[86]

Treatment.—When a patient learns that he does not have a seriously crippling, ankylosing disease, " he will go home greatly improved because you have dispelled his fears."[118] The usual remedies are recommended:[45] rest, reduction of trauma, dietary correction of obesity, physical therapy and, in selected cases, peri-articular and intra-articular injections of 1 per cent. procaine hydrochloride.[104] Despite its apparent inappropriateness in this disease, synovectomy reputedly gave surprising relief to twenty patients with knees which were " painful and disorganised " by osteo-arthritis.[47] Most workers[45] considered massive doses of vitamin D, removal of foci, injections of vaccines or chaulmoogra oil and fever therapy of little value.

Backache and Sciatica

The usual multitude of papers were concerned with the manifold causes of backache.[45] Detailed anatomic and clinical studies were made of the finer anatomy of the sacro-iliac joints. Basing his opinion thereon, one writer[37] concluded that in cases of acute and chronic sacro-iliac pain lumbar and sacral joints are " not subluxated nor slipped, but roughened by infection and impacted or locked at one extreme of the normal slight but real motion."

Manipulation was considered the best treatment; its technique was described. The clinical and laboratory features of ruptured intervertebral disc and methods for its diagnosis were again reviewed in a score of papers[45] concerning more than 200 new cases proved at operation. Several of the papers[6, 8, 32, 64, 79] were of special interest. Characteristic features were a history of trauma to the back (in 50 to 80 per cent. of cases), sudden or insidious appearance of low back pain, generally (in 92 per cent. of cases[64]) with sciatica. The latter was unilateral in about 80 per cent., bilateral in about 20 per cent. of cases, and was constant or intermittent. Symptoms also included kyphos or flat back, scoliosis, reduced Achilles reflex, sometimes sensory and motor changes. Diagnosis is made on evidence derived from spinal fluid (generally elevation of protein above 40 mg. per cent.) and spinograms made after injections of air or lipiodol. Laminectomy and removal of the protruded disc were successful in practically all reported cases. Recurrences of pain were few; post-operative deaths were rare. Hypertrophied ligamenta flava may produce symptoms and signs similar to those from ruptured discs;[3] the two conditions cannot be differentiated even by spinograms. This is immaterial as the treatment of both involves laminectomy. Successful results from removal of the enlarged ligaments in fifteen new cases were reported.[45] Details of 583 cases of lumbar spondylolisthesis were reported.[72]

An interesting association was reported[62] between sciatica, hepatic disease and jaundice. Five cases of "sciatic neuritis" were described which preceded the onset of hepatitis; when jaundice developed, the sciatic pain was completely or almost completely relieved.

Spondylitis

Spondylitis Osteo-arthritica.—An unusual case was described, that of a man aged fifty-six years with marked cervical osteo-arthritis and extensive bilateral ossification of stylohyoid ligaments.[19] Hanflig's (1936) method of treatment for cervical osteo-arthritis, repeated mechanical stretching of the neck, received further approval: "some measure of relief" was noted by all of ten patients so treated.[106]

Gout and Gouty Arthritis

Clinical Data.—Current literature might lead one to the belief that gout is leaving its old homestead in England and is catching

up with the descendants of the Pilgrims in the United States. With relative ease American clinicians on the alert for gout have collected an appreciable number of cases of classical gout within a short time. The hereditary factor remains elusive; it was present in only 10 per cent. of one series of cases.[24] As usual most patients were men, but women with classical tophaceous gout were seen.[103, 116] Two American negroes were affected.[16, 24] New data on the medicinal provocatives of gout were reported; acute attacks were said to be precipitated by thiamin chloride (vitamin B_1)[116] and by decholin;[14] salyrgan does not always provoke them.[49] Tophi affected 32 and 43 per cent. respectively of patients in two series.[49, 116] Of special interest was a case of severe tophaceous gout with flexion deformities of knees and fingers, and ankylosis of multiple joints; the condition somewhat resembled rheumatoid arthritis. Gout was the sole cause as demonstrated by pathologic examinations.[65] Data currently presented favouring the existence of irregular gout continue to be unconvincing.[45] Renal insufficiency affected 33 per cent. of twenty-one cases;[49] urate stones and gravel were not infrequent complications, and were occasionally discovered before the first attack of gouty arthritis.[103]

Laboratory Data.—Not sufficiently known is the fact that sedimentation rates are markedly elevated in many cases (but not always) during acute attacks and rapidly become normal thereafter.[45] It was again noted that the uric acid of whole blood was usually, but not always, elevated, and the pattern of hyperuricæmia bore no constant relationship to that of the gouty arthritis. One investigator[49] noted that uric acid in serum (from blood collected and allowed to clot under oil) is constantly higher and less variable than that in whole blood; tests on serum were therefore recommended as being more accurate.

Pathological Features.—Excellent studies on the pathology of gout were made on the case which resembled rheumatoid arthritis, and the findings were described in detail by word and micro-photographs.[65] The ankylosis was caused by extensive formation of pannus studded with urates.

Ætiology and Pathogenesis.—No new ideas on ætiology were reported. No evidence was found[103] to support the ideas that the hyperuricæmia results from a deficient excretion or diminished destruction of urates in the body. Several gouty patients both during and between attacks excreted more urates than did non-

gouty controls. Cyclic variations occurred not only in the excretion of urates but also in urinary volume and its chloride content, in body weight and in insensible loss of perspiration; these variations occurred among both gouty and non-gouty persons, but were more notable among those with gout. Changes in barometric pressure seemed to be related to these cycles.

Treatment.—A few additions to standard treatment were reported. Crystalline thiamin chloride (vitamin B_1) was given orally and parenterally (1 to 10 mg.—that is, 330 to 3,300 international units—daily) to twenty-five gouty patients. In most cases an acute attack was provoked by initial doses, but thereafter the frequency of attacks was presumably lessened in several cases although hyperuricæmia was not controlled.[116] Despite the older views of the inefficacy of colchicine as a prophylactic of acute attacks some physicians again are advocating its intermittent use between attacks as a substitute for cinchophen.[34, 103]

Uric Acid Problem.—By studying the offspring of Dalmatian hounds (" high uric acid excretors ") mated with collies (" low uric acid excretors ") it was found[113] that " high uric acid excretion " is inherited as an almost completely recessive, non-sex-linked character, dependent on the presence of a single pair of mendelising genes. The genes underlying the " high uric acid excretion " and those underlying the production of Dalmatian spotting are resident in independent pairs of chromosomes. Such studies could and should be carried out on gouty families, particularly on the offspring of the union of a gouty and a non-gouty person. Children and other relatives of patients with gout may demonstrate notable hyperuricæmia without (other) symptoms of gout.[49]

Psoriatic Arthritis

The percentage incidence of psoriasis was 2·6 among 1,000 cases of rheumatoid arthritis, but only 0·3 among 1,000 cases of osteo-arthritis;[26] hence the association of psoriasis and rheumatoid arthritis was considered " of real significance." Of the twenty-six patients with psoriasis and rheumatoid-like arthritis, twelve had features sufficient for a diagnosis of " classical psoriatic arthritis." Two patients with psoriatic arthritis were markedly relieved of articular symptoms during pregnancy.[42] Massive doses of vitamin D (average dose 300,000 units) were given daily for five to thirty weeks to nineteen psoriatic patients, only two

of whom had arthritis. Symptoms referable to the joints were not relieved, but the psoriasis cleared entirely in three cases, was markedly improved in seven, and unaffected in the rest.[45]

Menopausal Arthralgia

The characteristics of this condition as it affected fifty-three patients were described[38] and included freedom from symptoms referable to the joints until after artificial menopause, then the appearance of articular pain, stiffness and tenderness without swelling or deformity, normal sedimentation rates, aggravation of menopausal symptoms by thyroid therapy and relief of menopausal and articular symptoms by estrogenic substance, generally 10,000 or more international units of progynon B given intramuscularly twice weekly for several weeks.

Articular Physiology

By a modification of methods used to isolate chondroitin-sulphuric acid from cartilage physicians[71] obtained from synovial fluid a sulphur-free and phosphorus-free polysaccharide apparently identical with hyaluronic acid, the polysaccharide isolated from bovine vitreous humour, human umbilical cord and hæmolytic streptococci (Lancefield, group A). Its presence in the last-named seems significant in view of the possible relationship of these bacteria to diseases of joints. The theory was presented[10] that normal calcification of bone is maintained by an alternating ischæmia and hyperæmia, produced by the contraction and relaxation of muscles. Hyperæmia causes rarefaction, decalcification of bone and osteoporosis; a relative ischæmia produces consolidation of bone. When the circulation is maintained within normal limits, bone remains unchanged. If hyperæmia produces resorption of bone, the use of heat in certain osseous and articular conditions may be injurious.

Campaign against Rheumatism

During the year under review the progress made in the campaign against rheumatism in the United States was considerable, even though unspectacular. Chief sponsors of the campaign in this country are the American Committee for the Control of Rheumatism, allied to the "Ligue internationale contre le rhumatisme," and the American Rheumatism Association. Of the international campaign Sir William Willcox recently wrote: "The

movement has passed the dangers of infancy and now enters on the stage of vigorous youth." It is sincerely hoped that this " vigorous youth " will not, like so many others, be lost through the war. The officers and members of the American Rheumatism Association, having anticipated with great pleasure the opportunity of acting as hosts to the 1940 meeting of the International League, were deeply disappointed when it became necessary to cancel rather elaborate plans already made for the meeting, plans into which several of our oldest and largest medical and educational institutions and the governments of the States involved had enthusiastically entered. It is tragic indeed that the fine co-operation expressed through the activities of the League must be temporarily suspended, but it is confidently expected that the general campaign and the activities of the League, though retarded by the war, will be renewed with increased vigour afterward, so that the hope of its sponsors may be realised; that perhaps within a decade the rheumatic diseases can be largely brought under control.

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TUBERCULIN REACTIONS IN ANKYLOSING SPONDYLITIS COMPARED WITH THOSE IN OTHER RHEUMATIC DISEASES*

By G. ROBINSON, M.B.

Two independent sets of observations made at the Devonshire Royal Hospital have both suggested that tuberculin sensitiveness in cases of spondylitis ankylopoietica tends to excess. The phenomenon has been noted recently during von Pirquet testing of assorted rheumatic patients, and formerly[1] as part of a study of the disease itself. Moreover, such patients have sometimes been treated by vaccination with a fluid containing autolysed tubercle bacilli (the Ponndorf cutivaccine), whose effects in varying degree of flush, œdema and scaling resemble those of a tuberculin reaction. It was therefore thought desirable to determine whether ankylosing spondylitis is in fact associated with excessive tuberculin sensitiveness.

The background of ascertained fact with regard to tuberculin tests[2] in so far as it specially affects the results below may be recapitulated as (1) the general positiveness of our population and (2) the lower levels in the young, in females and in wasting disease.

The following procedure was adopted. Von Pirquet tests were performed and read at one, two and ten days by a single observer. Five insertions, made from above down on the volar surface of one forearm, consisted of nought, two, six, seventeen and fifty per cent. Old Tuberculin (Burroughs, Wellcome) in saline. The areas of swelling and flush were measured and noted at each of the three readings, and from the data thus obtained each patient's reaction was assigned to one of six classes—namely, 0 Negative, 1 Very Weak Positive, 2 Weak Positive, 3 Moderate Positive, 4 Strong Positive, 5 Very Strong Positive. Thus the figures 0 to 5 form a von Pirquet index, or rough quantitative estimate of the intensity of tuberculin response suitable for purposes of comparison.

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Table I. shows the results obtained by applying this method of testing to a group of assorted " rheumatics " on the one hand and to a group of ankylosing spondylitics on the other. No case which had ever received tubercle vaccine was included in the series.

TABLE I

Groups.	*Number of Cases.*	*Average Age.*	*Average vP Index.*
Male spondylitis ankylopoietica ..	45	36·6	3·33
Assorted male rheumatics	90	43·1	2·57

The spondylitic group is less prone to the feeblest type of reaction (0 and 1), and its index is also weighted by the occurrence of three times the frequency of very strong positives obtained in the control group. The distinction between strong and very strong positives was made on the presence of swelling in addition to flush in the 2 per cent. insertion. In spite of the adverse age difference, the spondylitic index is about 30 per cent. higher than the control index.

The likelihood of this result being due to chance has now to be considered. The frequencies of the six index numbers for control and spondylitic groups are set out in Table II.

TABLE II

vP Index.	*Frequency.*	
	Controls.	*Ankylosing Spondylitis.*
0	8	1
1	17	3
2	14	8
3	26	13
4	17	8
5	8	12
No. of cases	90	45

The arithmetic mean for the control group is 2·567 and for the spondylitic group is 3·333. The standard deviation for the control group is 1·43 and for the spondylitic group is 1·34.

The standard deviation of the difference between the means—

$$\sigma = \sqrt{\left\{\frac{(1\cdot43)^2}{90} + \frac{(1\cdot34)^2}{45}\right\}}$$

$$= 0\cdot25.$$

Hence the difference between the means

$$= \frac{3{\cdot}333 - 2{\cdot}567}{0{\cdot}25}\sigma$$
$$= 3{\cdot}07\sigma.$$

Reference to probability tables shows that mere chance could produce the difference existing between the means in less than three out of a thousand occasions. One may conclude, therefore (though the number of spondylitic cases is fairly small), that the difference is significant and not due to chance, and that the fact of increased sensitiveness to tuberculin occurring in the spondylitic group is thereby established.*

The control group was composed of the following cases:

Fibrositis	28
Subacute rheumatism	20
Osteo-arthritis of spine	11
Osteo-arthritis of other joints	9
Gout	9
Sciatica	6
Paget's disease	3
Gonoccocal arthritis	2
Subacute combined degeneration	1
Paraplegia	1
	90

All were ambulant, and nearly all in good condition. Cases of rheumatoid arthritis were excluded, since their general health was impaired and since it was found that their von Pirquet index was low, approximating to that of the females tested, who themselves showed no material difference between rheumatoid and non-rheumatoid levels, as evidenced in Table III.

TABLE III

Groups.	*Number of Cases.*	*Average Age.*	*Average vP Index.*
Male rheumatoid arthritis	19	43·3	2·1
Female „ „	44	43·8	2·0
Other female rheumatics	53	42·6	1·9

* Grateful acknowledgment is due to Dr. Duncan Black, University College of North Wales, for checking this calculation.

Thus the two diseases, ankylosing spondylitis and rheumatoid arthritis, which show a number of similarities, are contrasted in respect of their tuberculin reactions.

One patient in the spondylitic group had undergone orchidectomy fifteen years before (cause not ascertained). In the male control group, three gave histories of possible tuberculosis in themselves and five in their families. No clinical evidence of tuberculosis was present in any patient tested.

In order to investigate the tubercular specificity, or otherwise, of the spondylitic skin reaction to tuberculin, the evidence of the tuberculin complement fixation test as to the presence

TABLE IV

Age.	*Disease.*	*Reading.*	
		Parke, Davis Antigen.	*Saline Suspension Antigen.*
47	Ankylosing spondylitis	0	0
31	,, ,,	0	0
40	,, ,,	0	–
34	,, ,,	0	0
33	,, ,,	0	0
19	,, ,,	0	0
41	,, ,,	0	0
37	,, ,,	0	0
32	,, ,,	0	0
35	,, ,,	0	0
51	,, ,,	0	0
37	,, ,,	0	0
43	,, ,,	0	0
27	Phthisis	+±	+
31	,,	±	±
30	,,	+±	+
16	,,	0	0
41	,,	Anticomp.	
26	,,	+	+±
25	,,	+	+
55	,,	+	+
49	,,	+	±
33	Subacute rheumatism	0	0
26	,, ,,	0	0
30	,, ,,	0	0
35	Rheumatoid arthritis	0	0
27	Fibrositis	0	0
62	,,	0	0
40	,,	0	0
42	,,	0	0
35	,,	0	±
35	Osteo-arthritis of spine	0	0

or absence of actively antigenic tubercle was employed. Each serum was given two separate tests on the same day: one with Parke, Davis* antigen and one with a saline suspension of a strain recently isolated from sputum and killed by steaming. The tests were based on the M.R.C. No 1 method for the Wassermann and proved conservative, no strong positive (++) readings being obtained. They were discontinued after thirteen out of thirteen clear negatives had been obtained from the sera of spondylitics, and seven out of nine positives from the sera of phthisis patients.† Table IV. (p. 44) gives the readings.

The results of the von Pirquet and complement fixation tests combine, therefore, to indicate a tuberculin sensitivity which may not be specifically tubercular in spite of the fact that typical and not pseudo skin reactions occurred, and in spite of the fact that control experiments with *B. coli* "tuberculin" (*i.e.*, concentrated glycerine broth culture of this organism) failed to elicit abnormal responses. Nor could the strength of the tuberculin reaction be correlated with any other factor in the course of ankylosing spondylitis, except, imperfectly, with the patient's level of health: those whose constitutions were most impaired, and among whom loss of flesh (but not necessarily of function) was greatest, comprise the majority of the sensitive class.

Discussion

Evidence explaining the above results is not forthcoming. They might reflect either a non-specific irritant in the tuberculin or a subclinical tubercular state in the patient. The only form of subclinical tuberculosis recognised is the immunising infection of young adults ; and it is not impossible that a more intense tubercular baptism than normal might predispose some cases to the inheritance of spondylitis. Previous histories of subacute rheumatism and of spinal fracture are not uncommon in ankylosing spondylitis; fluorine poisoning[3] can cause an identical bony buttressing of the column ; and cases of Paget's disease (one in the present series) are known to have occasionally developed typical bamboo spines. All these conditions, together with the healing of tuberculosis, involve change in calcium metabolism ; and one of the most essential of early signs in ankylosing spondylitis is decalcification of bone.

* Given by the firm.

† Kindly supplied by Dr. Capes of Bishopstoke Sanatorium.

SUMMARY

1. The tuberculin sensitiveness of forty-five patients with ankylosing spondylitis has been found to be 30 per cent. higher than that of ninety rheumatic control cases.

2. This result is statistically significant since there is only a 0·3 per cent. chance of its being due to random sampling.

3. Negative tubercular complement fixation reactions in thirteen cases of the disease show that the skin reaction has no background of actively antigenic tubercle detectable by this test.

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SPLENECTOMY IN THE TREATMENT OF RHEUMATOID ARTHRITIS*

A REPORT OF THREE CASES

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At a meeting of the Royal Medical and Chirurgical Society in 1896 Dr. George Still read a paper on "A Form of Chronic Joint Disease in Children." He described a form of chronic polyarthritis of childhood beginning before the second dentition, and characterised by chronic progressive enlargement of joints without bony change and by general enlargement of the glands and of the spleen.

In 1924 Dr. A. R. Felty published a paper in the Johns Hopkins Hospital Bulletin entitled "Chronic Arthritis in the Adult associated with Splenomegaly and Leukopenia." He described five middle-aged patients, three men and two women, suffering from chronic arthritis, with enlargement of the spleen, leukopenia and enlarged lymphatic glands. In every case a yellowish-brown pigmentation of the skin was noticed. All were undernourished and gave a history of marked loss of weight since the onset of symptoms. In every instance the arthritis was long-standing, and the spleen was palpably enlarged, firm but not tender. There was a slight anæmia and a leukopenia, the white cells varying between 1,000 and 4,000 per cubic millimetre. Two of the patients ran a low fever for some weeks. Dr. Felty appears to have been uncertain whether to classify these cases as an adult form of the syndrome described by Still, or as two separate entities—Banti's disease and chronic arthritis—occurring concurrently in the same individual. He presented them as examples of a distinct clinical entity of unknown origin.

In 1930 Dr. Paul Chevallier wrote in the *Revue de Médecine* an article on "La Maladie de Chauffard-Still et les Syndromes Voisins." He gave a detailed account of the ætiological and clinical aspects of this syndrome. He emphasised its similarity

* Received January 20, 1940.

to " le rhumatisme bilaire " of Gilbert and Fournier and the arthritic manifestations of Hanot's " cirrhoses bilaires." He described the ineffectiveness of the various forms of medical treatment, and in his final paragraph noted that, as far as he knew, in no instance had the spleen been removed. " It might be worth trying. It is a known fact that in patients with splenic enlargement the associated symptoms often abate after removal of the spleen. Although such results of this kind would be incomprehensible at present, it is not impossible that the operation might bring about a regression of the arthropathies."

In 1932 Dr. Hanrahan and Dr. Miller reported from Baltimore the result of a splenectomy which they had performed on a patient presenting this clinical syndrome. Their patient was a woman of fifty years of age, suffering from a chronic arthritis, in whom a large spleen and liver, a slight secondary anæmia, and leukopenia of about 1,000 cells per cubic millimetre was noted. Following the removal of the spleen, they claimed that there was a marked improvement in the condition of the affected joints which became less painful and less stiff, and also the white cells rose to 10,000 per cu.mm. Five months after the operation this improvement was maintained. The spleen was found to weigh 525 grammes. Microscopically no specific changes were noted, although there was a great hyperplasia of the endothelial cell lining, dilated sinuses, and increased numbers of plasm cells in the pulp spaces.

In 1934 Dr. Erle Craven of Durham, North Carolina, presented a detailed report on a similar case. The patient was a woman of forty years of age, with a rheumatoid type of arthritis of five years' duration. The first clinical manifestations occurred some nine days after a normal pregnancy. Adenopathy and splenic enlargement were noted. There was anæmia with 3,000,000 red cells, 2,500 white cells and a low-grade pyrexia. Following removal of the spleen, there was a striking subjective improvement with increased mobility of the hands, elbows, knees, and ankles. When reviewed some eight months later, however, little permanent improvement was noted. The spleen weighed 620 grammes and revealed much the same histological picture as in the former case.

In 1935 Dr. Reginald Fitz presented at a clinical meeting at the Peter Bent Brigham Hospital, Boston, a man sixty-three years of age, who presented the clinical picture of Felty's syn-

drome. He was treated medically, but died soon after of a short illness suggesting a coronary thrombosis or pneumonia. While discussing this patient Fitz stated that both Hanrahan's and Craven's patients had died within eighteen months of the removal of their spleen.

In 1937 Loeper, Lemaire and Patel reported in the *Presse Médicale* a case under their care at the St. Antoine Hospital, Paris. The patient was a woman twenty-eight years of age. She had an advanced rheumatoid type of arthritis of seven years' duration. Splenic enlargement, a diffuse adenopathy, an anæmia with 3,480,000 red cells per cu.mm., and a leucocyte count of 6,800 per cu.mm. were noted. The patient was treated medically with drugs and blood transfusions without improvement. Finally the spleen was removed. There was an immediate marked subjective improvement with diminution of pain and swelling and increased joint movement. She continued to improve until, unfortunately, thirty-five days after the operation she developed a broncho-pneumonia and died. The spleen weighed 610 grammes, and the histological picture was similar to that in the previously recorded cases.

The authors state that "splenectomy transformed the patient's pitiable condition within a few days." There was a sudden and marked improvement in the general condition, and a gradual return to full function of the joints, the digital joints alone remaining deformed and a little stiff. They pointed out that in this disease one is probably concerned with diffuse mesenchymal reaction involving the synovial membrane, the capsule of the joints, the muscles, the spleen and the lymphatic glands characteristic of an infective disease. Although tuberculosis, syphilis and other infections had been held responsible for its ætiology, every laboratory investigation, biopsy of the synovial membrane, study of the articular fluid, and examination of the spleen had given negative results. They suggested that if the Chauffard-Still syndrome might be looked upon as being one of the "recticulo-endothelioses," a vast framework to include the arthritic forms of Hanot's disease and the primary splenomegalies with glandular enlargement or arthropathies, then, though the ætiology be unknown, a reason would be given for the clinical improvement following splenectomy. They suggest that if the spleen be regarded "as the essential site of the disease, and if the 'arthropathising' rôle (Alessandrini) is attributed to

its involvement, one might wonder if this organ liberates certain substances having a very weak action, but to which a previously allergic individual might react very strongly in certain preferred sites."

Later in 1937, Dr. Villaret and others presented a case at a meeting of La Société Médicale des Hôpitaux de Paris. The patient was a woman forty-two years of age with advanced rheumatoid arthritis of seven years' duration, slight splenic enlargement, a diffuse adenopathy, and anæmia with 3,800,000 red cells and 9,000 white cells. Intensive medical and physical treatment resulted in but little clinical improvement. The spleen was removed. On the day after the operation there was a marked decrease of pain and diminution of swelling in the affected joints, and there followed a gradual but marked improvement in the general condition of the patient. Immediately prior to the operation the white cell count was 21,000 per cu.mm.; ten days after the operation it was 15,000 per cu.mm.

We do not know the ætiology of the rheumatoid type of arthritis, nor are we prepared to conjecture as to the rôle of the spleen in this disease. In this paper we propose simply to report in some detail the case histories of three patients who during the last year have been under our care in the Rheumatic Unit at St. Stephen's Hospital (L.C.C.). They are all suffering from the rheumatoid type of arthritis. In each, after extensive but unsuccessful medical, physical, and in one case operative treatment, the spleen was removed.

Case 1.—Rheumatoid type of arthritis—a young woman aged eighteen. Occupation none. Admitted to the Rheumatic Unit under our care on February 18, 1938.

Past History.—She is a twin whose brother is perfectly healthy. Until the age of nine she was well and won prizes at baby shows. When she was nine years old the joints of the fingers became swollen, and she began to lose weight rapidly and ran a temperature. She was admitted to St. Mary's Hospital, where a diagnosis of Still's disease was made.

After a year's treatment she was quite well and running about. She went to school until the age of thirteen, when again she began to lose weight, had pain and swelling of the knees, feet and hands and a rash with fever.

She was readmitted to St. Mary's under the care of Professor Langmead, who has kindly given us a summary of her condition at that time:

"Patient ill and anæmic—swelling of the left wrist, which was hot, painful and limited in movement. Metacarpo-phalangeal joints of the left hand swollen and painful; movement in shoulders somewhat restricted; knees stiff. Considerable kyphosis. Spleen palpable one inch

below costal margin. Epitrochlear glands palpable. Few small soft glands in both anterior and posterior triangles of neck. Large soft glands in both axillæ and hard glands in the groins.

"Pulse rate 100, B.P. 100/60. Soft apical systolic murmur. The patient suffered from rashes and a swinging temperature, often rising to 103. Duodenal catherisation revealed a streptococcus from which a vaccine was made. No abnormality was found in the blood or stools. X-ray report showed no evidence of bony change nor reduction of cartilage spaces."

After six months she was sent to Margate Hospital, where the right leg was put in extension. At the end of a year she could walk, but with stiff knees.

Aged sixteen : She was at home and walking a little. The general health was good.

Aged seventeen : Two months before admission there was a severe relapse with fever and pain and increasing stiffness in all the joints, including the temporo-mandibular.

On Examination.—February 18, 1938. A pale, emaciated girl lying stiffly in bed. She was not in severe pain, and could only open her mouth a few degrees. T. 98·4° F., P. 100, R. 20. Weight 4 st. 3 lb. The spleen was not palpable and there was no adenitis. The range of movement in the hands, wrists, elbows, shoulders and neck was restricted to some 20 per cent. of the normal. The hips were fixed in flexion and the knees were flexed with less than 10 per cent. of normal movement.

Laboratory Investigations :

Blood count :

R.B.C.: 4,120,000.	W.B.C.: 12,200.
Hb.: 58 per cent.	Polymorphs: 89·5 per cent.
C.I.: 0·7.	Lymphocytes: 7·5 per cent.

Blood culture: Sterile.
Sedimentation rate: 53 mm. fall at end of first hour (Westergren).
Wassermann reaction: Negative.
Gonococcal fixation test: Negative.
Blood calcium: 9·7 mg. per 100 c.c.
Blood phosphorus: 3·6 mg. per 100 c.c.

Radiography.—All bones show generalised rarefaction. Marked cartilage destruction in all joints except the sacro-iliac joints where there was no evidence of fusion.

A diagnosis was made of the rheumatoid type of arthritis in an advanced and active phase.

Treatment.—A high caloric semi-solid diet was a necessity owing to the difficulty the patient had in opening her mouth. A course of neosolganal (Schering), calcium-gold-keratinate with 14 per cent. of gold, was begun with 0·01 gm. intramuscularly. After the second injection of 0·02 gm. there was a severe reaction. T. 103°, P. 140, and general malaise. The blood count showed a leucopenia of 2,000, polymorphs 74 per cent., lymphocytes 19 per cent. This leucopenia was treated with adrenaline subcutaneously, pentnucleotide intramuscularly and blood transfusions. Within six days the leucocytes had risen to 6,400, and after six weeks the pyrexia was lower and the general condition improving.

Two months later, with the object of relaxing the generalised muscular spasm, a posterior plaster shell was made including the head and supporting the body down as far as the knees. The patient remained in the plaster shell for six months, during which time she had physical treatment—general ultra-violet light, massage and gentle movements of the joints.

At the end of this period the general condition had improved and there was a gain of 10 lb. in weight, but there was very little improvement in the joint condition and the sedimentation rate remained at its previous high level.

It was decided to perform a splenectomy in the hope of arresting the disease.

October 25, 1938.—Mr. S. W. Holmes removed the spleen under spinal anæsthesia through a left paramedian incision. The spleen was found to be twice the normal size and to be bound down by avascular adhesions. There were no splenunculi.

Pathological Report.—The splenic tissue shows the changes of amyloid disease.

The post-operative course was uneventful. Gradually throughout the ten months following this the general and local conditions have improved.

Eight months later the patient had improved sufficiently to go to a convalescent home for one month, and there could walk half a mile and climb a few stairs with the aid of crutches. Following this she was allowed to go home.

August 24, 1939.—Afebrile. Weight 5 st. 6 lb. No pain. The jaw movement was still restricted to 10 per cent. of normal. In the neck, shoulders, elbows, wrists, knees and ankles there was at least 50 per cent. of the normal range of movement and in the hips 20 per cent. of the normal.

Investigations :

Blood count :

R.B.C.: 5,240,000.	W.B.C.: 12,500.
Hb.: 80 per cent.	Polymorphs: 58 per cent.
C.I.: 0·9.	Lymphocytes: 34 per cent.

Sedimentation rate: 32 mm. fall at the end of first hour.

This was a case of the rheumatoid type of arthritis occurring in a young girl. At its onset it fulfilled the criteria for a diagnosis of the Chauffard-Still disease.

Gold therapy had to be discontinued owing to the tendency to leucopenia, and other methods of treatment failed to improve the condition.

After splenectomy and removal of an amyloid spleen there was no dramatic change, but since that time improvement has been steady.

Case 2.—Rheumatoid type of arthritis. A young man aged eighteen, by occupation a clerk. Admitted to the Rheumatic Unit on April 10, 1938, under our care.

Past History.—On two occasions within the previous nine months he had had attacks of joint stiffness, once in the left shoulder and once in the knees, in each case lasting a few days and not causing him to leave work. He had had no sore throats before, and apart from measles and whooping-cough as a child had no illness. No history of venereal disease.

Present Illness.—One month before admission he had a sore throat and general malaise. The large joints became painful and swollen, and within two weeks he was unable to stand.

On Examination.—A pale, thin boy, lying in pain and unable to move. T. 100·4°, P. 100, R. 25. Soft discrete glands were palpable in the epitrochlear and inguinal regions. The spleen could not be felt. The skin was moist and atrophic and there was marked wasting of the limb muscles. There was gross periarticular swelling of the interphalangeal, wrist, elbow, knee and ankle joints. All movement was painful and limited by muscle spasm around the joints. The pharynx was injected—tonsils not enlarged—sounds normal. B.P. 130/85.

Laboratory Investigations : Throat swab—non-hæmolytic streptococci.

Blood count :

R.B.C.: 3,920,000.	W.B.C.: 9,300.
Hb.: 62 per cent.	Polymorphs 67 per cent.
C.I.: 0·7.	Lymphocytes 27 per cent.

Blood culture : Repeated several times yielded a growth of *S. fæcalis alkaligines* on one occasion only.
Sedimentation rate: 66 mm. fall at end of first hour (Westergren).
Wassermann reaction: Negative.
Gonococcal fixation test: Positive.
Urethral smear and prostatic bead (repeated): No pus; no organisms.
Electrocardiogram: No abnormalities.
Blood uric acid: 2 mgm. per 100 c.c.

Radiography.—Generalised rarefaction of bone with commencing erosion of the articular cartilages of the wrist joints. No gross changes in the elbow or knee joints.

A diagnosis was made of the rheumatoid type of arthritis in an active phase.

Treatment.—Rest in bed. High caloric diet and six tablets of Multivite each day. (Vitamin A, 3,000; B, 50; C, 200; D, 600 units per tablet.) Sodium salicylate gr. xx, two-hourly by day, four-hourly by night for fourteen days. There was no improvement either in the joint pains or general condition.

At this stage light plaster shells were made to support the hands, wrists, knees, and ankles and to prevent deformity. Next iodoseptine (iodo-benzo-methyl-formin-42 per cent. iodine) was given intramuscularly, 10 c.c. each day for fourteen days. There was no improvement; the muscle wasting was increasing and the joint movement becoming increasingly restricted. Serial radiographs showed increasing erosion of cartilage.

May, 1938.—One month after admission a course of neosolganal was given by weekly intramuscular injections of 0·05 gm. After the sixth injection albuminuria was detected and the gold was stopped. The urine was sterile on culture and with an occasional granular and hyaline cast. Within ten days the urine was clear of albumen and no casts or cells were seen.

Following this, two fresh methods of treatment were tried—blood transfusions and arthrotomy and lavage of each knee.

June, 1938.—The patient was transfused with 300 c.c. of citrated blood, and this was repeated three weeks later. Iron therapy was continued and the blood picture improved.

July 8, 1938.—R.B.C.: 5,560,000, Hb.: 87 per cent., C.I.: 0·8, W.B.C.: 9,300.

May 27, 1938.—Arthrotomy and lavage performed on the left knee, and June 24 on the right knee by Mr. A. G. Timbrell Fisher. After each operation there was a fall of temperature for ten days. It then reverted to the former level of 99° to 101°.

Operation findings were similar in each knee. The joint was full of necrotic fibrinoid material of which about 8 oz. could be easily expressed. The synovial membrane was congested and œdematous. Beyond early pannus encroaching on to the edges, no change was seen in the articular cartilages. The joints were irrigated with Dakin's solution and closed without drainage.

July 8, 1938.—Prontosil 0·5 gm. in tablet form was given four-hourly for ten days. There was no change in the clinical condition, nor was the pyrexia diminished.

By this time, two and a half months after admission and three and a half months since the onset of the illness, the condition of the patient was gradually becoming worse. There was persistent pyrexia (99° to 100·4°), extreme muscle-wasting and restriction of movement in all joints. The range of movement in the elbows, wrists, knees and ankles was less than 10 per cent. of normal. The blood sedimentation rate remained raised.

All forms of therapy tried (salicylates, Iodoseptine, gold, arthrotomy, and lavage, transfusions, and prontosil) had failed to arrest the progress of the disease. It is felt that there was insufficient or no evidence to suggest that *Streptococcus fœcalis alkaligines* or the *gonococcus* played an ætiological rôle.

In order to relieve the pain and spasm around the joints it was decided to try the effect of splenectomy.

August 16, 1938.—The operation was performed by Mr. S. W. Holmes, under general anæsthesia. The spleen was found to be twice the normal size. There was no perisplenitis.

Pathological Report.—Moderate œdema and congestion and slight excess of leucocytes in the spleen.

The post-operative course was uneventful. Fourteen days after the operation the fever tended to lessen. There was no marked improvement following splenectomy, and two months later the boy's father insisted on taking him home against advice.

June, 1939.—The boy was visited in his home by one of us (O. S.) and examined. Though the general condition was extremely poor, it was no worse than when he left hospital, and there were clinical signs that the rheumatoid arthritis had become quiescent. There was no fever nor peripheral sweating and no pain at rest or on movement. In the fingers, wrists, elbows, shoulders, hips and ankles the movement was 10 per cent. of normal. There was none in the knees.

It is probable that had this boy been able to have continued orthopædic and physical treatment while the disease was becoming quiescent, the result would have improved. Even with partial ankylosis the joints are in the optimum position owing to early splinting.

Case 3.—Rheumatoid type of arthritis. A young woman aged twenty-nine years. Occupation, children's nurse. Admitted to Rheumatic Unit under our care on April 21, 1938.

Past History.—Eight years ago: The right hand suddenly became swollen and painful. This subsided after three days but recurred later. Within two years all the large joints had become affected and she was getting about only with difficulty. She came under the care of one of us (F. J. B.) at the St. John Clinic, when a diagnosis of the rheumatoid type of arthritis was made. She was treated with intra-pelvic diathermy and the joints improved, but she was not able to go back to work.

Five years ago : Admitted to the Westminster Hospital for six months. Tonsillectomy was performed, the hands were supported with plaster shells and physical treatment given. The left leg was stiffened at the knee and a caliper worn for some months.

Three and a half years ago : Readmitted to the Westminster Hospital. At that time radiography showed no sign of anylosis, and the joint spaces were reported as being " fairly good."

One year ago : A course of gold injections was given, and this resulted in some improvement until after two months she developed a rash on the face, with a yellow nasal discharge, and the gold was stopped.

A second course was started some months later, but this was terminated after four months, as the pains were worse.

Four months ago : Admitted to Lewisham Hospital where a course of prontosil was given.

During her illness, apart from the joint pains, she had felt well, and there had been only slight loss of weight. The menses had been irregular ever since the onset.

On Examination.—A well-nourished girl lying in constant pain. T. 98·4°, P. 82, R. 22. There was cyanosis of the cheeks, lips, fingers, and toes, and the hands and feet were moist. There were no enlarged lymph glands nor was the spleen palpable. Movement in all joints was limited: in the wrists to 10 per cent., and in the elbows, shoulders, right knee, and ankles to 30 per cent. of the normal. The left knee was stiff. The most marked feature was the degree of muscle spasm which resulted from passive movement of any joint, especially those of the lower limbs. There were also painful involuntary attacks of spasm in the quadriceps muscles.

Apart from the joints no clinical abnormality was found. B.P. 120/75.

Laboratory Investigations :

Blood count :

R.B.C.: 5,160,000.	W.B.C.: 8,700.
Hb.: 64 per cent.	Polymorphs 52 per cent.
C.I.: 0·6.	Lymphocytes 32 per cent.

Sedimentation rate: 57 mm. fall at end of first hour (Westergren).
Spectroscopic examination of blood: Sulphæmoglobinæmia.
Wassermann reaction: Negative.
Gonococcal fixation test: Negative.
Blood uric acid: 1·9 mgm. per 100 c.c.
Test meal: Achlorhydria.

Radiography.—Partial ankylosis of the carpal joints, some destruction of the heads of the metacarpals. Other joints show narrowed joint spaces and cartilage erosion.

A diagnosis was made of the rheumatoid type of arthritis in an advanced and active phase.

Treatment.—Complete rest, a high caloric diet and analgesics for the pain. Light plaster supports were made for the hands and right leg.

May, 1938.—Ten million T.A.B. was given intravenously, resulting in a fever of 104° F. The peripheral sweating was much reduced after this and the joints were looser for five days only. This was followed by ionisation with histamine to the hands and feet and gentle movements of the joints, but no improvement resulted and there was still as much pain.

June 24, 1938.—In the hope of relieving the painful spasms and increasing the joint movement, bilateral lumbar sympathectomy was performed by Mr. Holmes. The spasm was relieved to some extent, but there was still great pain on any movement.

July, 1938.—A course of solganal B was given by weekly intramuscular injections until 1·76 gm. had been given. At the same time, on the advice of Mr. Philips, the consulting gynæcologist, endocrine therapy with progeston and menformon was begun. During this time the general condition improved, but there was no change in the joint function nor relief of pain.

Eight months after admission and following treatment by protein shock, gold, physical methods and sympathectomy, there was little improvement and the sedimentation rate remained high.

It was decided to try splenectomy in the hope of relieving the pain and improving the joint condition.

December 12, 1938.—Under general anæsthesia, Mr. K. F. D. Waters removed the spleen, which was enlarged to twice the normal size and was bound down with dense adhesions.

Pathological Report.—The spleen shows the changes of amyloid disease.

The post-operative course was uneventful. Since splenectomy there has been a very slow but sustained improvement. Eight months later she was able to walk 100 yards with little pain and was sent for a month's convalescence, during which she improved considerably. Following this, she had been admitted to a training school in order to learn needlework so that she may earn her living again.

September, 1939.—She can walk several hundred yards and climb a few stairs without pain. She can use her fingers well, and there is an increased range of movement in the wrists, elbows, shoulders and right knee to 50 per cent. of the normal range. Peripheral sweating is absent and the involuntary muscle spasms are very occasional.

Laboratory Investigation :

Blood count :

R.B.C.: 5,600,000.	W.B.C.: 10,340.
Hb.: 96 per cent.	Polymorphs 60 per cent.
C.I.: 0·9.	Lymphocytes 25 per cent.

Sedimentation rate: 28 mm. at end of first hour.

It is well known that surgical intervention such as tonsillectomy or cholecystotomy for the removal of possible foci of infection in patients suffering from the rheumatoid type of arthritis may be followed by transient clinical improvement. Some temporary diminution of pain and joint deformity may occur. Whether this is due to the removal of a specific causative factor, or to the

production of non-specific protein shock with stimulation of the reticulo-endothelial system, or to the period of rest and controlled dieting that follows an operation, we do not know. In our opinion the improvement in the clinical picture which may follow splenectomy is of quite another character and is probably not explainable along these lines. Although we may offer certain reasons for the clinical improvement, we do not feel that as yet they are sufficiently well defined to be included in this description of our cases.

SUMMARY.—Three cases are described in which splenectomy was performed for the rheumatoid type of arthritis; in two cases amyloid change was found. They have been followed for a period of over nine months in each case. In two of the cases marked clinical improvement has followed the operation, and in the other, although there is no clinical improvement, the disease appears to have become quiescent. The literature on the subject has been reviewed.

We are indebted to Sir Frederick Menzies, Chief Medical Officer to the London County Council, for permission to publish the case reports.

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THE SPONTANEOUS POLYARTHRITIS OF RATS AND THE SYNDROME INDUCED BY INOCULATION OF HUMAN MATERIAL IN THESE ANIMALS*

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Translated by G. J. PETHER, M.D., M.R.C.P.

Though the joint changes of rheumatic fever are striking, the cardiac lesions are even more important. Both the cardiac and the visceral lesions may develop without any changes in the joints, analogous conditions obtaining in the polyarthritis of rats. In these animals the polyarthritic form of the disease is that most commonly encountered, the disease being first noted in the foot, then spreading up the leg, being first a mono- and later a polyarthritis, spreading from one limb to another.

In our investigations it seemed as though some "arthrotropic" agent was at work in the early stages, but later there is a partial or total cessation of the active joint changes though the infective agent could be recovered from the joints, the internal organs, or both. Certain cases occurred in which, though the inoculation was made through the skin and the joints escaped, the infective agent was nevertheless recoverable from the internal organs as demonstrated by further animal inoculation. The condition of these animals was regarded as one of latent infection, since they showed no symptoms of disease whatever.

Various other strains found in the spontaneous disease of rats have been isolated and fully reported elsewhere. Variations were noted in the proportion of animals which showed joint changes after the inoculations with various strains, but the same strain had always about the same proportion of joint lesions. It seems reasonable to assume that each strain has a viscerotropic tendency present in greater or less degree. The two tendencies correspond

* Received October, 9, 1939.

to those noted in the hypothetical agent of rheumatic fever in man, but the joint changes in the rat disease are very unlike those seen in human beings.

Joint Changes in the Spontaneous Disease in Rats

We here give a short review of the X-ray changes seen in the rat following disease started in the foot. The animals were killed and X-rayed at suitable intervals, but the bones are so small that examination is difficult, and a magnifying-glass does not overcome the distortion caused by the grain of the X-ray film.

The striking joint changes are quite unlike anything seen in man, for rheumatic polyarthritis in man is notable for the slight X-ray changes. The soft tissues are swollen and the joint space may be widened, but the appearance is otherwise normal. With prolonged rest a slight atrophy may develop. In other forms of arthritis, atrophy and bone destruction are striking.

In rats, from the beginning there is marked hypertrophic change in the affected joints, with strong bony outgrowths from the periosteum and grotesque exostoses resembling those seen in neuropathic arthritis (Charcot's joints). These may appear in as short a time as fourteen days. The hind-paws usually suffer most, the tibia showing periosteal thickening and outgrowths developing round the ankle joint, the bones here collapsing to a formless mass. The thickenings and osteophytes may be seen in the metatarsal bones and phalanges (see Fig. 3 and compare with 1 and 2, which are normal).

Though the hind-limb suffers most, this is apparently not due to the fact that the infection starts here, for the joint lesions rapidly become generalised and the organs contain the infective agent after a few days. It may be admitted that the local trauma from the insertion of a cannula has provided a "locus resistentiæ minoris," in which a preponderating amount of the infecting agent is located, but this factor must not be overrated. Changes are seen in the joints of the fore-paw, periosteal thickenings of the radius and ulna, and irregular deformity of the metacarpals and thickened phalanges (Fig. 4). The knees may be attacked and show a picture resembling arthritis deformans. In some cases a marked coxitis is seen in which the socket of the joint is largely destroyed. This may cause a luxation (Fig. 5). The elbow joints are not often involved (Fig. 6), but in a few cases the vertebræ of the tail may be affected (Fig. 6). Hitherto

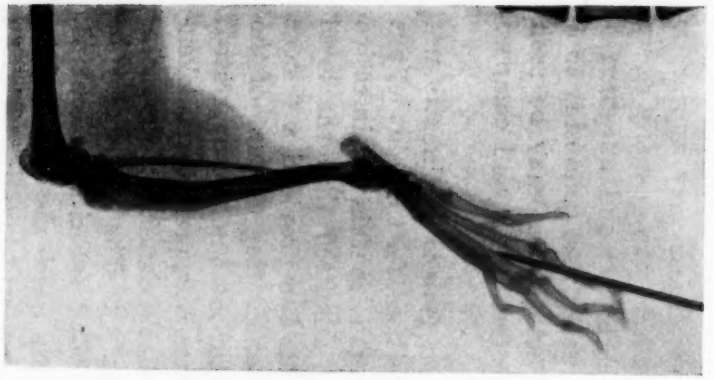

FIG. 1.—NORMAL HIND-LEG.

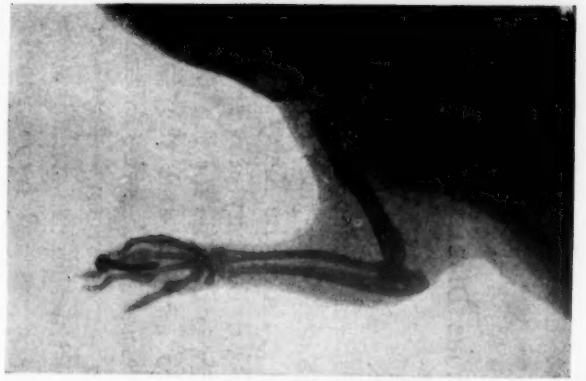

FIG. 2.—NORMAL FORE-LEG.

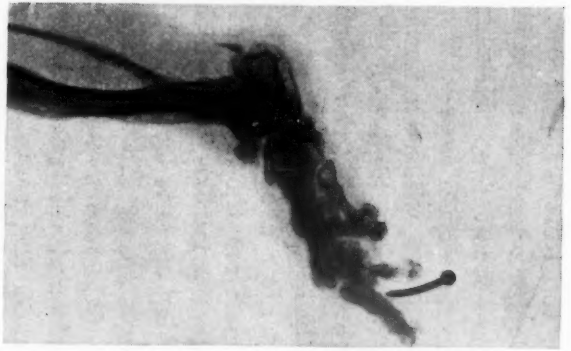

FIG. 3.—HIND-LEG SHOWING PATHOLOGICAL CHANGES.

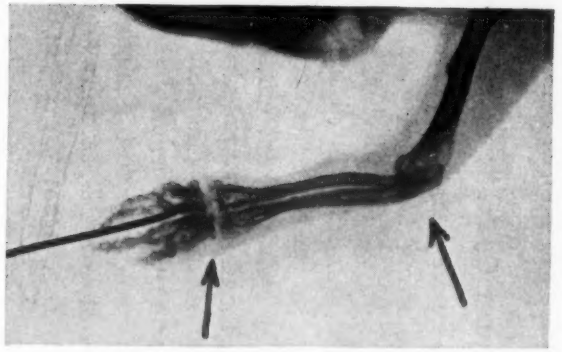

FIG. 4.—FORE-LEG, PATHOLOGICAL.

FIG. 5.—DISEASED KNEE AND FOOT.

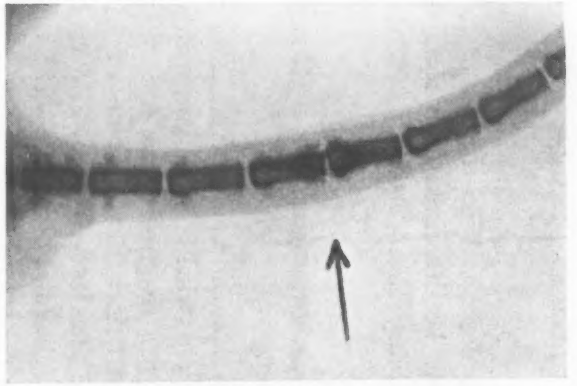

FIG. 6.—CHANGES IN JOINTS OF TAIL.

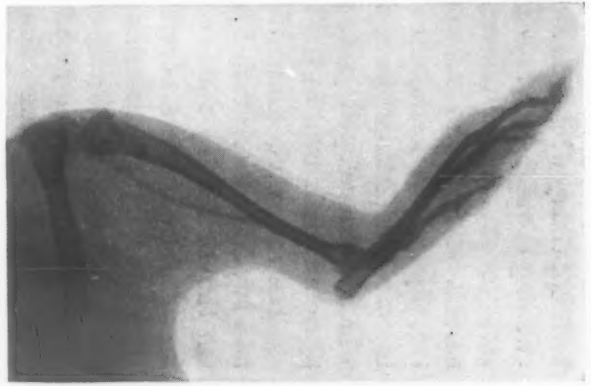

FIG. 7.—"OEY" STRAIN, FIRST PASSAGE.

FIG. 8.—"OEY" STRAIN, SECOND PASSAGE.

no involvement of the shoulder joints or mandible has been noted.

The changes described can rarely be demonstrated clinically. The lesions in the tail seem to be independent of the site of the inoculation. The changes seen may be described as a form of hypertrophic osteo-arthritis resembling those seen in arthritis of neuropathic origin.

Changes Seen in the Joints after Inoculation of Human Material

The strain chosen for this investigation was derived from a patient suffering from rheumatic polyarthritis with pericarditis and pleurisy. He died later, and the diagnosis was confirmed post mortem. Twenty-four hours before death some of his citrated blood was inoculated into the feet of ten white rats; half an hour before death some pericardial puncture fluid was inoculated into another ten rats, and ten minutes before death another sixteen rats were given plantar inoculations of fluid taken from the joints.

The first rat to show symptoms had been inoculated from a joint, and this was killed after forty-nine days, having developed a swollen joint. Further inoculations from it were made into a series of thirty white rats. Only one of these showed any marked swelling of the joints, and inoculation from it into another twenty rats gave negative results. Another animal which had been inoculated from the patient's joint also exhibited swelling of a tarsal joint. This animal was killed on the ninety-first day, and further inoculations from it were made into another ten rats, which all developed joint swellings. This strain may be used again and is known as the Oey joint strain.

Ten rats were inoculated with pericardial fluid, but only one had swelling of the tarsal joints and this was somewhat atypical. On the 102nd day further inoculations were made from it into fourteen rats, some of which developed joint swellings which were not very characteristic. On the 111th day further inoculations were made with negative results.

The results of the blood inoculations are, however, of special interest. Of the ten animals to which these were given only one was made ill at the outset. Seventy days later re-inoculation from this one was made into a series of thirteen rats in the foot. All of these were markedly affected. On the seventy-seventh day

a further inoculation was made from them into another ten rats, which all became ill, and this strain may be carried further. After an interval another animal in the series inoculated from the blood was taken ill, and on the 102nd day re-inoculations from it were performed into another fourteen rats, all of which became ill and were used for further inoculations. This parallel passage was certainly capable of further transmission (strain Oey, blood 2).

It was thus possible to inoculate from one patient in three different ways, once with joint exudate and twice with citrated blood, and all three methods exhibited a relatively low proportion of affected cases, the incubation period being unusually long with a marked increase in virulence. There was no clinical difference between the conditions which developed and the spontaneous disease of rats, the method of spread appearing to be the same.

X-ray investigations were made in a series of white rats which had been inoculated with joint fluid from a rat exhibiting joint changes after inoculation with blood. The animal was killed on the seventieth day (strain Oey, blood 1, passage 2). These animals were killed at weekly intervals and X-rayed, while animals suffering from spontaneous rat polyarthritis were used as controls.

The marked increase in virulence in the second passage was seen to be associated with a change in the nature of the joint lesions; in Fig. 1 the slight joint changes on the seventieth day are such as would be seen in human beings. Only the soft tissues are involved and no bony change has occurred. But in the second passage bony changes are noted and are similar to those of spontaneous rat polyarthritis. By the seventh day there is some bone atrophy, and on the fourteenth a marked periostitis is noted, becoming later an osteo-chondritis as in the rat disease. The changes become more marked in the following weeks, and are quite like those of spontaneous rat polyarthritis, the other extremities are involved and in six weeks an obvious coxitis is seen. No other joint lesions were noted, but perhaps the time for observation was too short.

On close observation one sees some slight differences between the spontaneous rat disease and that developing after inoculation of human material. In the latter the bone atrophy is more marked throughout, while the hypertrophic and destructive changes are not so evident. Nevertheless there is little real

difference between the two syndromes, and the X-ray findings definitely support the clinical impression of a close similarity between the two conditions.

Discussion of the Results

It seems possible that the human disease is transmitted to rats, but sources of error must be eliminated.

1. An endogenous origin of the disease in the inoculated rats seems unlikely since white rats have not hitherto shown such changes.

2. It is possible that a latent infection of the rats was lit up by the inoculation material. Against this it must be noted that in the course of numerous experiments no latent infection of the white rat has yet been observed. No spontaneous disease has been found, nor in the passages has such been seen to appear. Tissue extract from apes and rats has been injected into many hundreds of these animals without the development of morbid changes. Inoculation with material from other human beings did not cause any symptoms to appear. There is every reason to believe that the white rats bred at the Eijkman Institute are free from any spontaneous infection.

3. Transmission from contaminated syringes is impossible since new and unused needles were used invariably.

4. Complete confusion of one condition with the other seems unlikely, since several rats inoculated from the same patient showed joint changes.

5. The possibility of an unknown carrier having transmitted the disease is unlikely. Only animals in the cages directly inoculated were affected, all those in other cages remaining free. We could not even find evidence to show that diseased animals could infect other healthy ones in the same cage; even direct contact had no effect.

The spontaneous polyarthritis of rats first identified in Batavia has been found in London by Findlay, Mackenzie, MacCallum and Klieneberger in the rat colonies of three Institutes. There were slight differences in behaviour in these, such as the discovery that the condition could be transmitted to mice. The authors mentioned that half-grown rats had a shorter incubation time and larger animals a longer one, while full-grown rats were quite resistant. We did not observe such points in our own rats. The polyarthritis in the London rats appeared to be endemic, while

no such disease prevailed in the Eijkman Institute. In the latter no spontaneous outbreaks occurred and the adult animal was not immune. The absence of such immunity is of interest since this normally is found after the disease has run an obvious or an occult course; for this reason it would appear that the activation of a latent rat disease in our cases is most unlikely. This is even more evident when it is remembered that attempts to transmit other diseases from man and from monkeys and other white rats have not caused any joint conditions to become active.

Findlay claims to have identified organisms of the pleuro-pneumonia group known as L7 in the endemic rat arthritis as seen in London. Dr. Klieneberger informs me that she has also grown the same organism from the rat polyarthritis strain from Batavia. We have not repeated her work here as yet, as the facilities are lacking and difficult to provide in the tropics. Other organisms of the pleuro-pneumonia group are indicted as causing arthritis in mice (Klieneberger 1936, 1938), both in the L7 and L5 series.

Findlay has found a strain known as L6 in the brain of normal mice which is capable of producing arthritis, and Sabin reports a similar L5 strain having similar effects.

Pigoury has found a pleuro-pneumonia organism which he considers responsible for the agalactia of goats, and in 10 to 20 per cent. of these cases arthritis develops.

We see then that in a whole series of cases there is an organism of the pleuro-pneumonia type. The rat family has possibly a special sensitivity to this type of organism, and it might be thought that the Oey strain was one of human rheumatic fever which had been transmitted to the rat.

It is interesting to note the initial slight virulence and the later greater degree thereof after the second passage, though this is commonly seen. It occurs in relapsing fever when inoculated from man to mice, and in the series first inoculated there is very rarely relapse, but in subsequent inoculations the typical course is run.

Organisms have been found in pleuro-pneumonia which can excite polyarthritis, and similar organisms can be found in cases of arthritis in human beings and in rats. It is reasonable to suggest that the same strain may be found in human beings and in rats. We have hitherto suggested that the pleuro-

pneumonia-like organisms are themselves responsible for the appearance of the disease, but this is not quite proven. Such have been found by Seiffert and Orskov and by Laidlaw and Selford in all sorts of places and all sorts of dirt. They have likewise been identified in normal animals.

It is also possible that the organisms resembling those of pleuro-pneumonia convey a virus which can be grown in tissue cultures. This is a characteristic peculiar to the exciting organisms of arthritis.

Summary

Spontaneous arthritis of rats is a hypertrophic osteo-arthritis which may attack all joints in varying degree. The marked degree of hypertrophy is uncommon in man and resembles the gross changes seen in tabes and syringomyelia. When material from a patient with rheumatic polyarthritis had been inoculated into rats there was noted in the second transmission (passage) a clinical and X-ray picture indistinguishable from that seen in spontaneous polyarthritis of rats. The possibility of a true transmission of the human disease to the rat is discussed.

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The paper on "Rat Fleas and Rheumatism" (Clarke, J. Tertius, *Proc. Roy. Soc. Med.*, 1928, xxi., Sect. Epidemiology, 48) is of interest in the light of these investigations.—Editor.

THIRD ANNUAL REPORT OF THE EMPIRE RHEUMATISM COUNCIL

(To organise research throughout the British Empire into the causes, and means of treatment, of Rheumatic Disease)

My Lords, Ladies and Gentlemen,

On account of the war, which has called away for service many of our members, and entails on most of the others difficulties in travelling, your Executive Committee considered that it would be in accordance with your wishes that the Annual Meeting should not be summoned this year. I shall not, therefore, have the pleasure of addressing you personally, but now present the Annual Report to October 31, 1939, noting that, if any member wishes to bring up a matter arising out of the Report, prompt attention will be given to it by the War Emergency Committee which has been constituted; and should there arise any question needing discussion at a general meeting (which I do not anticipate) a meeting will be summoned.

Last year, at this time, you will recall that we were able to chronicle satisfactory progress, though the period under review had been disturbed by constant rumours of war. All hope of escaping the calamity of war has proved vain. Faced with the alternative of seeing the fabric of European civilisation destroyed piecemeal, the British Empire, side by side with France, has been compelled to take up arms.

Since September your executive officers have devoted themselves to planning how to save, as far as possible, the work of the Council from interruption and at the same time to conserve our resources so that when peace returns the campaign against rheumatism may be carried on again with full vigour. The need at that time will be certainly greater than heretofore. We shall, almost certainly, have to face an increased incidence of Rheumatic Disease arising not only from the war casualties but from a degree of interruption of normal health services to the civil population.

You will be chiefly interested in our plans for the war period; but, before referring to them, I must give a brief record of the developments of our movement up to September last.

That development was so promising as to make its interruption specially tragic. First, there was manifest a strong growth of public interest in, and public determination to grapple with, the problems of Rheumatic Disease. This was shown notably at the meetings of the Rheumatism Section of the Annual Congress of the Royal In-

stitute of Public Health and Hygiene in the spring, and at meetings of various associations of the Approved Societies under the Health Insurance Act in the summer. At these meetings there was expressed strong sympathy with the aims of our Council. In April our President, H.R.H. the Duke of Gloucester, at a Mansion House meeting (the Lord Mayor of London presiding) stated those aims admirably, and expressed his full confidence that the peoples of the British Empire would bring them to success.

Secondly, we had good reason to be satisfied with the extending scope of our research work, and with indications which justified the hope that it was on the way to gaining definite results.

Thirdly, we were on the point of bringing to a successful issue several negotiations for the increase of centres for adequate treatment.

Thus, on all three fronts of our campaign against rheumatism—the education of the public; the research into causes; the remedying of the national scandal that only a percentage of sufferers can secure the treatment which, in many cases, would save them from lapsing into crippling disability—there was good progress.

That progress has been seriously interrupted, and, to some extent, the interruption must continue until peace comes.

There will be no captious criticism on our part, nor, I think, from any reasonable quarter, founded on the presumption that precautions were excessive at the outset of hostilities. It had to be recognised that we were entering into war against an enemy led by a personality who is altogether ruthless, and whose actions are, for pathological reasons, largely incalculable. There is little doubt that if the enemy had not been, at the outset, disappointed of the support relied upon from two powerful quarters, there would have been attempted the "lightning stroke." In that case, ruthless air attacks on London and other of our cities might have given ample employment to the emergency casualty services, for the organisation of which so much of the normal medical needs was sacrificed. Fortunately, events imposed upon the enemy a policy of timidity, and suggested to him the alternative tactic of playing for a kind of peace so that a better opportunity of mass attack might be sought later.

May we not take advantage of that and, without abandoning the measure of war precaution which present circumstances dictate, make some progress towards the normal measures of defence against those enemies which never pause in their attack—the agencies of disease?

In the treatment of Rheumatic Disease we know that, before the war, our national facilities were gravely deficient. As a consequence of the war emergency measures, they have been further reduced to a very considerable degree. Yet neglect of the rheumatic sufferer will inevitably bring a harvest of post-war cripples, not victims of shot and shell, but of Home conditions.

The Council's Treatment Work

It is in the matter of treatment that there has been the gravest interruption of your Council's work. The Rheumatism Ward at the Hospital of St. John and St. Elizabeth has been temporarily closed; also the Rheumatism Clinic at the West London Hospital, in the establishment of which the Boroughs of Kensington, Hammersmith and Fulham co-operated with the Empire Rheumatism Council. These two centres were the first fruits of the Council's work to remedy the lack of facilities for rheumatism treatment in the kingdom. Added to their loss is the suspension, for the time being, of negotiations—in one case on the point of completion, in other cases far advanced—for important new provincial centres. There are, however, two good facts to record. The rheumatism treatment centre at Edinburgh, under Professor Stanley Davidson, which is helped by our Scottish Fund, is continuing its work; also the St. John Clinic and Institute of Physical Medicine in South-West London is still carrying on.

But to state the full extent of the national loss of centres for rheumatic treatment since September, it is necessary to note the experience of other institutions not so directly linked with our Council, but working in co-operation with it, a co-operation which was developing in scope. The British Red Cross Clinic (the largest of London's treatment centres) has closed its doors.* The Spa hospitals, in peace-time chiefly devoted to Rheumatic Disease, have been largely diverted from that purpose. I have not sufficient data on which to found a close estimate of the degree of interruption of such rheumatic treatment as was available at the General Hospitals in their out-patient and in-patient departments before the outbreak of war, but, undoubtedly, it has been very great.

So far I have referred to the treatment of adult rheumatism only. In regard to the treatment of juvenile rheumatism, there has been also grave interruption. Prior to this war, Great Britain had reason to be proud of the fact that the London County Council scheme for the prevention and treatment of Rheumatic Disease among school children was the best probably in the world; and a few other British municipal administrations had systems approaching it in efficiency. The dispersal of a large proportion of school children from industrial to rural areas has interrupted to a large extent the working of the London and other schemes. It will be recognised that that was unavoidable. Safeguarding the young from anticipated bombing attacks on the great cities was of paramount importance. But we may urge that a considered effort should be made by the national authorities to apply to children transferred to rural areas, in the degree

* The British Red Cross Clinic has since reopened (February, 1940).

that is possible, the health precautions which had been doing so much to shield them from disease.

Last year I noted that the task of preparing a report on a system of treatment which might be economically applicable to a large number of sufferers, and even possible of application on a national scale, was actively proceeding. The report had been brought near to completion, but the constantly deepening national anxiety in regard to the international position did not offer a favourable opportunity to bring it forward. Now it must await the return of peace.

The report of Dr. Tegner, holder of the Sir Alexander Walker Travelling Scholarship, on the work of Rheumatism Treatment Centres in Europe and North America, was presented in July and published in full in the fourth number of our official journal, ANNALS OF THE RHEUMATIC DISEASES, and members will agree that it is a valuable record and analysis of foreign systems of treatment.

Your officers have formulated plans to place at the disposal of the defence authorities the scientific resources of the Council in dealing with the incidence of Rheumatic Disease in the fighting services during the present campaign ; these will be put forward when the appropriate time comes.

THE COUNCIL'S RESEARCH WORK

Happily, interruption of our Council's research work has been much less serious than that of treatment work. At first it was feared that practically all research would have to be suspended because of the taking over of hospital premises for war casualties and the calling up of workers for services. Later, with the absence of massive bombing attacks on London and other centres, it was found that most of our research work could be continued after a very brief interruption. To note in some detail the position on October 31.

The work of the Frederick Pearson—Sir Halley Stewart Foundation for research into the incidence of Rheumatic Disease in the training establishments of the Royal Navy seemed doomed to suspension, owing to the mobilisation of the Navy and the transference of some naval medical establishments. As the state of development of the work was highly promising, strenuous efforts were made to avoid this, and I wish to acknowledge the sympathetic help given by Surgeon Vice-Admiral Sir Percival Nicholls, Director of Naval Medical Services, in the matter. We can hope now that the work will be continued under Dr. C. A. Green at naval establishments. The section of the work under Professor Ernst Freund and his assistants at the West London Hospital has not been interrupted. The assistance given at Edinburgh University by Professor T. J. Mackie,

and at Glasgow University by Professor J. W. McNee, will, we hope, continue.

Work at the Sir Alexander Maclean Laboratory, the Hospital of St. John and St. Elizabeth, London, under Dr. C. B. Dyson, has been suspended temporarily, and also the work there of investigating the value of Occupational Therapy in the treatment of arthritis. This was made necessary by the national plan for taking over hospital accommodation for war emergency casualties.

Work at the Sir Alexander Maclean Laboratory at the Pimlico Clinic of the Order of St. John, under Dr. H. J. Taylor, is being continued.

Work by Dr. E. G. L. Bywaters, in support of which the Empire Rheumatism Council is co-operating with the Beit Fellowship, at the British Post-graduate Medical School, University of London, is being continued.

Work by Professor E. Freund at Edinburgh University is being continued.

Work by Dr. C. Lutwak-Mann at the University of Cambridge is being continued.

Work by Dr. L. Michaelis at the Orthopædic Department of the St. John Clinic is being continued.

Our official journal, ANNALS OF THE RHEUMATIC DISEASES, I may note here, has, during the year, made a remarkable contribution to the literature of Rheumatic Disease, having published many notable articles, including a particularly valuable paper from Professor Aschoff (the discoverer of the "rheumatic node"). I trust that members of the Council will do their utmost to extend its circulation, though, during the war period, for purposes of economy, we may have to limit the number of issues.

During the course of the year under review there was brought to the notice of our Research Advisory Committee promising results recorded by scientists of the Pilsudski University, Warsaw, in regard to a serological test for acute rheumatism. Action was at once taken to get into touch with those scientists and to support experimental work in this country in order to confirm their results. Professor Mackie of Edinburgh University and Dr. J. E. McCartney of London have both undertaken to investigate this matter. Unfortunately, we must presume that the research work of the Pilsudski University, Warsaw, has been suspended now that Poland is under the yoke of the invader. But when Poland is restored we may hope that contact can be resumed and this research work continued. The Polish scientists had promised to contribute to our official journal a record of their most recent results and to supply material for test purposes.

The Chemical Sub-Committee of the Scientific Advisory Com-

mittee has instituted an investigation of gold therapy in rheumatoid arthritis, with a carefully planned system of controls and provision for independent assessment of clinical results and of statistical check. This Sub-Committee consists of: F. J. Bach, D.M.; W. S. C. Copeman, M.D., F.R.C.P.; Professor L. S. P. Davidson, M.D., F.R.C.P., F.R.S.E.; Professor F. R. Fraser, M.D., F.R.C.P.; S. J. Hartfall, M.D.; Professor J. W. McNee, D.S.O., M.D., F.R.C.P.; W. S. Tegner, M.R.C.P.; E. C. Warner, M.D., F.R.C.P.; Lionel Whitby, C.V.O., M.D., F.R.C.P.; Sir William Willcox, K.C.I.E., C.B., C.M.G., M.I., F.R.C.P. The work had just begun when war intervened. Some delay must now be anticipated in bringing it to a conclusion.

Dr. Green, Director of the Naval Research Foundation, represented the Empire Rheumatism Council at the Third International Congress for Microbiology, New York, and was invited to contribute a paper which, we have learned, aroused great interest. The report he has presented of the proceedings of this Congress is valuable for its notes on information concerning current research in rheumatism in the United States.

Organisation Development

The check to organisation development has been great. Australia had arranged during the coming year a National Medical Congress on Rheumatic Disease at which a Council affiliated to, and with the same objectives as our own, was to be founded. That has been postponed.

Negotiations for the formation of two provincial Councils in the Home Country have had to be put aside for the present. In these matters, as in others referred to, the policy of your Executive has been to keep in mind that postponement does not mean abandonment, and that, as soon as circumstances permit, efforts in regard to these developments will be resumed.

On October 11, 1939, the Executive Committee of your Council decided to vest all its powers temporarily in a War Emergency Committee, consisting of Lord Horder, G.C.V.O., F.R.C.P.; Sir William Willcox, K.C.I.E., C.B., C.M.G., M.D., F.R.C.P.; A. G. Timbrell Fisher, M.C., F.R.C.S.; Mervyn H. Gordon, C.M.G., F.R.S., D.M.; T. W. Robinson, A.C.A.; Sir Walter Kinnear, K.B.E.; and W. S. C. Copeman, F.R.C.P.

Throughout the year your Committees and officials have given devoted zeal to the work of the Council, and I am confident that if you were assembled in the usual manner you would unanimously re-elect them, and express sincere thanks for their services. I shall be pardoned, I know, if I do not attempt to catalogue all who have given great service, but confine particular mention to Sir William Willcox, who has carried out the two onerous tasks of Chairman of

the Executive Committee and Chairman of the Research Advisory Committee; Dr. Mervyn Gordon, Chairman of the Scientific Advisory Committee, who is indefatigable in promoting the scientific activities of the Council; Mr. T. W. Robinson, who, as Chairman, and Sir Walter Kinnear as Member, of the Finance Committee, have given untiring zeal to the great responsibility of keeping us on the straight financial path; Mr. Timbrell Fisher, one of the Trustees; Dr. W. S. C. Copeman, the Hon. Medical Secretary, now on active service in France, but still continuing to give devoted attention to our work; and by no means last, though coming last in this list, Sir Frank Fox, O.B.E., who has given the Council invaluable service.

It is proposed by the War Emergency Committee that the standing Committees should remain as at present constituted, but that they be not summoned for meetings during the war period unless some special need arises. As soon as peace returns the Committees will be asked to resume their functions, and at a general meeting of the Council you will be invited to elect them anew.

I shall leave it to the Finance Committee to report to you on the funds of the Council, only commenting that prudent policy in the past has allowed us to go through a gravely troubled year without financial embarrassment.

In conclusion, let me thank the generous and public-spirited subscribers to our campaign and express the earnest hope that sufficient financial support will be forthcoming during the war period, from present supporters and from others, to ensure the continuance of the Council's research work and its efforts to promote new treatment centres. In his inspiring speech at the Mansion House in April last our President, the Duke of Gloucester, stated: "We in this country have never allowed a necessary and urgent task of this kind to be neglected because of difficult times." We must justify His Royal Highness's confidence. The War on Rheumatism must be waged until victory is gained over a group of diseases which inflict on the community so much suffering and financial loss.

(Signed) HORDER,
Chairman of the Council.

1, Mitre Court Buildings,
Temple,
London, E.C. 4.

ACTA RHEUMATOLOGICA

THE "Ligue Internationale contre le Rhumatisme," with which the Empire Rheumatism Campaign is affiliated, has been compelled to suspend its activities for the duration of the war and its journal, *Acta Rheumatologica*, suspended publication in December, 1939. The Empire Rheumatism Council has offered to publish from time to time in the ANNALS news and announcements which would otherwise have appeared in the *Acta*, and the Editors will be glad to receive communications, and to publish them as far as space will permit. A list of recent publications and articles from the medical journals of many countries on the subject of rheumatism has been received from Dr. van Breemen and will be included in an early issue of the ANNALS.

The Seventh International Congress on Rheumatic Diseases was to have taken place under the auspices of the League in America in June, 1940, but has had to be postponed. The President elect, Dr. Ralph Pemberton of Philadelphia, has circulated a pamphlet among the members explaining the postponement and giving an account of the programme which had been prepared, and with it a letter from which the following extracts have been taken:

"Certain misapprehensions seem to have arisen regarding the present status of the League. It is therefore deemed important for me, as President of the League, to state that I have never, in this official capacity, approved of any action which would create the impression that the League was dissolved, nor could I in my capacity as President take any step, without the collaboration of the membership as a whole, which might result in the dissolution of the League.

"It is morally certain that if the League were to be dissolved an attempt would be made sooner or later upon cessation of hostilities to recreate it. . . . It is therefore believed by many in the United States that the creative efforts of Dr. van Breemen over the years, which have resulted in the League and the successful meetings held by it, should not be allowed to lapse. Furthermore, it seems of the highest importance in the present state of world affairs that every line of affiliation and co-operation should be kept available for use at the earliest moment. . . . It is the opinion of the American Rheumatism Association that the present structure and personnel of the League should be maintained, in a condition of suspended animation if necessary, for the duration of the war, ready to resume activities as soon as circumstances permit."

The Empire Rheumatism Council hope that by providing space in the ANNALS for news of the League it may be of service in promoting the objects advanced by Dr. Pemberton on behalf of his colleagues in America.